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CENTER FOR THE FUTURE OF CHILDREN • THE DAVID and LUCILE PACKARD FOUNDATION

The Future of Children

VOLUME 5 • NUMBER 1 - SPRING 1995



LOW
BIRTH
WEIGHT

Statement of Purpose

The primary purpose of *The Future of Children* is to disseminate timely information on major issues related to children's well-being, with special emphasis on providing objective analysis and evaluation, translating existing knowledge into effective programs and policies, and promoting constructive institutional change. In attempting to achieve these objectives, we are targeting a multidisciplinary audience of national leaders, including policymakers, practitioners, legislators, executives, and professionals in the public and private sectors. This publication is intended to complement, not duplicate, the kind of technical analysis found in academic journals and the general coverage of children's issues by the popular press and special interest groups.

In this issue of *The Future of Children*, we focus on the seemingly intractable problem of preventing death and disability in infants as a result of being born too soon at low birth weight. This topic is important because (1) low birth weight results in significant loss of life—with the years of unfulfilled potential that early death represents for each child and for society; (2) many surviving infants sustain residual injuries that often tragically involve the central nervous system; (3) the children and their families often endure pain and suffering; and (4) there are substantial financial costs involved. Over the past three decades it had been hoped that a number of health and welfare programs, whose primary objectives were to provide needed medical services to pregnant women (such as prenatal care) or to ameliorate harmful effects of poverty on children (such as WIC), would also, coincidentally, prevent the onset of most preterm labor and delivery. This has not occurred. Therefore, based on current knowledge, further interventions are needed. These should include providing women of reproductive age with additional health services before pregnancy. Because cigarette smoking during pregnancy significantly increases the likelihood of having a moderately low birth weight baby, there also should be intensive programs to discontinue smoking during pregnancy. Programs directed at discouraging children and adolescents from starting to smoke would also have a beneficial effect on reducing the low birth weight rate.

In addition to these measures, a significantly greater research priority should be given to investigating the mechanisms controlling the onset of labor. Further, two-fold black to white (and Asian) racial differences persist in the prevalence of preterm labor, low birth weight, and infant mortality, and these outcomes are not adequately explained by socioeconomic or lifestyle variables. Consequently, particular attention should be given to possible biological factors that might contribute to the increased vulnerability of black women to having the premature onset of labor. It is our hope that by redirecting attention to this subject, further progress can be made in reducing preterm delivery of low birth weight infants early in the 21st Century.

The articles presented here summarize knowledge and experience in selected areas that we believe are relevant to improving public policies in the United States that have an impact on infant mortality and morbidity. We hope the information and analyses these articles contain will further understanding of the important issues and thus contribute to reasonable changes in policies which will benefit children.

We invite your comments and suggestions regarding this issue of *The Future of Children*. Our intention is to encourage informed debate about preventing the preterm birth of low birth weight infants. To this end we invite correspondence to the Editor. We would also appreciate your comments about the approach we have taken in presenting the focus topic and welcome your suggestions for future topics.

Richard E. Behrman, M.D.
Editor

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The next issue of *The Future of Children*
will focus on long-term outcomes of early
childhood programs.

Low Birth Weight: Analysis and Recommendations

Analysis

Each year more than four million families in the United States bring home from the hospital a healthy baby who has all of the potential for a full and productive life. The birth of a baby is a joyous event, and the baby's survival is taken for granted. But one family in 100 will suffer the loss of their child soon after birth. Why are these 40,000 babies dying each year? As Paneth discusses in his article, more than three-quarters of infant deaths are caused by babies being born too small or too early. The occurrence of these infant deaths is highly correlated with size at birth and length of gestation; the proportion of deaths increases with decreasing birth weight and gestation. Low birth weight is the term used to define infants who are born too small, and preterm birth is the term used to define infants who are born too soon.¹ In 1991, 7% of all infants in the United States were born too small, and 11% were born too soon. This journal issue takes an in-depth look at what is known and what is not known about the major underlying cause of infant mortality and childhood morbidity—low birth weight.

For the past quarter century, the United States has ranked poorly in international comparisons of infant mortality. In 1993, the United States ranked 22nd in the world in infant mortality, well behind Japan, Singapore, Germany, and most Scandinavian countries.² The reasons for the relatively high rates of infant mortality in the United States are unknown. It seems incongruous that, compared with newborns in other countries, so many more American infants die. The United States has one of the most advanced medical care systems in the world, superbly trained medical care providers, and nearly univer-

sal access to medical care for pregnant women. Yet, in international comparisons, United States infant mortality rates remain relatively high. Paradoxically, the United States is unsurpassed in its ability to rescue the very smallest infants. Because of advances in neonatal care systems, many infants who weigh only 750 grams (1 pound, 10 ounces) at birth are now surviving.³ However, these successful rescue efforts are often associated with significant long-term health and developmental problems among survivors⁴ which limit their opportunities to lead full and productive lives.

Medical scientists have focused on two major strategies to find ways to reduce the number of infant deaths: improving the survival of low birth weight infants and preventing low birth weight and preterm delivery. As is described below, the success of these two strategies has been mixed.

Although the United States has relatively high infant mortality rates in international comparisons, infant mortality rates in this country, like those in most other countries, have been declining. In the past two decades, infant mortality rates have declined substantially while rates of low birth weight and preterm births have remained virtually stable (see Figures 1–6 in the article by Paneth). How can these very highly correlated outcomes—infant mortality and low birth weight—have taken such different paths? The seemingly contradictory decline in infant mortality without parallel declines in low birth weight or preterm birth is attributable to the increasing survival of low birth weight infants. Horbar and Lucey note in their article that improvements in neonatal intensive care and drug therapies to help very preterm babies breathe outside the womb are responsible for much of the decline in infant deaths in the past 10 years. But how far can we expect technology to take us in reducing the number of infant deaths in the United States and at what cost?

These life-saving technological advances have a price. As efforts to save small infants improve and become more widely available, the associated medical expenditures increase. A very tiny baby often must stay in the hospital intensive care unit for months and requires constant care and attention. Hospital bills for rescuing only one of these tiny babies can reach more than one million dollars. Most of the dollars spent on low birth weight infants are devoted to saving a small group of very tiny infants. Lewit, Baker, Corman, and Shiono estimate in their article that, of the \$11 billion spent on health care for infants today, approximately 35% (\$4 billion) of these dollars are spent on the incremental costs of low birth weight infants, with

nearly half going to rescue the very tiniest babies (\$1.8 billion).

The stable rates of low birth weight and preterm delivery suggest that prevention efforts have been frustrating and unsuccessful. Advances in determining the causes of low birth weight and increases in the utilization of prenatal care have been insufficient to change the stubbornly stable course in the rates of low birth weight and preterm delivery. Researchers know why some babies are born too small but have been unsuccessful in applying this knowledge to reduce the number of low birth weight births. Up to 20% of all low birth weight births could be prevented if no pregnant woman smoked cigarettes (see the article by Chomitz, Cheung, and Lieberman). However, the causes of most preterm births have not been identified.

In studying the problem of low birth weight in the United States, epidemiologists have described a disturbing and as-yet unexplained phenomenon. As Paneth states in his article, “Equal opportunity for life is an American ideal that is unfulfilled even at birth.” African-American babies are twice as likely as white infants to be born low birth weight, to be born preterm, and to die at birth. Only 17% of all births

In 1993, the United States ranked 22nd in the world in infant mortality, well behind Japan, Singapore, Germany, and most Scandinavian countries.

are to African-American families, yet 33% of all low birth weight births and 38% of all very low birth weight births are to African-American families. Little is known about why African-American infants are at such high risk of adverse birth outcomes. Many believe that scientists must take a fresh look at this problem and approach it from a different vantage point.

This issue of the journal takes an in-depth look at one particular topic, low

birth weight infants. This analysis begins by examining recent successes in reducing the infant death rates in the United States, summarizes current knowledge about the long-term health and developmental outcomes of low birth weight children, and determines if and how low birth weight can realistically be prevented. It ends with policy recommendations about specific steps that should be taken to reduce the occurrence of low birth weight and infant deaths.

Medical Care for Low Birth Weight Infants

Improving Survival

Horbar and Lucey document in their article tremendous advances in the development and utilization of neonatal intensive care treatments and drugs which have improved the survival of the tiniest babies in the past two decades. This same period has also witnessed improvements in the availability and accessibility of neonatal intensive care, and the advent of neonatal and perinatal subspecialists who are trained to care for the very tiny infant. Together, these advances have provided the capability to rescue a good proportion of the smallest infants.

The development, refinement, and availability of neonatal intensive care have been credited with saving the lives of many infants. While it is not known exactly how many babies have been saved by these means, marked declines in infant death

all infants in the country access to neonatal intensive care. Finally, the decline in infant deaths in the past five years is attributed to the introduction of surfactant therapy, which makes it easier for very small infants to breathe outside the womb and reduces their susceptibility to serious lung disease.

McCormick and Richardson discuss how regionalized care was designed to provide expensive, high-level care for very sick infants in an effective and efficient manner. In a regionalized system, one neonatal intensive care unit is responsible for all of the infants from a large geographical area who require intensive care. This large population base helps to guarantee an adequate volume of patients and to assure both efficiency and quality of care. Regionalization also improved access to care by providing a centralized place for the care of all neonates within a region. No definitive studies have been conducted which document whether or not regionalization of neonatal intensive care was effective. However, there is indirect evidence which shows a sharp decrease in infant deaths after the introduction of regionalized care.

Recent trends toward deregionalization of neonatal intensive care services have resulted in the rapid proliferation of community-based care units. This increase in the number of neonatal intensive care units, particularly in suburban areas, has been stimulated in part by the fundamental changes in the way health care is organized and financed in the United States. The growth of large managed care health insurance providers has fueled the ongoing competition among providers and hospitals to attract insured families. It appears that some neonatal intensive care units are being established to attract young, insured families by assuring them that high-level infant care is available in their communities. An increase in the number of intensive care facilities in local communities may increase access to care, particularly for insured families. But large-scale deregionalization also has the potential to dismantle the current system of regionalized care. How these changes will affect the availability and distribution of neonatal intensive care is unknown.

The Limit of Survival

As the limit of survival is moved to smaller and smaller infants, many questions are raised about how neonatal intensive care

Of the \$11 billion spent on health care for infants today, approximately 35% (\$4 billion) of these dollars are spent on the incremental costs of low birth weight infants.

rates have coincided with the introduction of neonatal intensive care and with its refinements. Horbar and Lucey note that three lines of evidence support the notion that neonatal intensive care saves lives. First, low birth weight infants born in hospitals having the highest level of neonatal intensive care are much more likely to survive than are infants born in hospitals having lower levels of care. Second, the development of a system of regionalized care for the very smallest infants who need the highest level care has allowed nearly

technologies should be used. Currently, most infants born at 24 or more weeks of gestational age survive. One study reported that before 24 weeks, very few infants survive; at 23 weeks, only 15% of infants survive; and at 22 weeks, almost no infants survive.³ Tyson discusses in his article the difficult ethical questions health care providers, families, and society face when they must decide if an infant is so sick that neonatal intensive care should be stopped or not administered. While these ethical questions are certainly not new, recent advances in medical technology, which are often achieved at high cost, have brought these difficult questions to the forefront. More needs to be known about the decisions to initiate care, to identify when an infant is not responsive to care, and to withdraw care when necessary.

Tyson notes that current federal child abuse regulations mandate care for all live-born infants unless the infant is irreversibly comatose or is in a condition where treatment would be “futile” and merely prolong dying or would be “virtually futile” and inhumane. The withholding of medically indicated care is defined as child abuse and neglect. Unfortunately, the precise definitions of futile or inhumane are not provided, and the law gives no practical guidance for clinicians and families who must make these difficult decisions. Tyson argues that this law is much too simplistic and that a number of factors must be considered in deciding how to care for the very smallest infants. These factors include the probability of survival, pain and suffering, future quality of life, and the economic cost of care.

Long-Term Outcomes for Low Birth Weight Infants

Hack, Klein, and Taylor note that, while a large majority of low birth weight infants are normal and healthy, as a group they have higher rates of subnormal growth, adverse health conditions, and developmental problems. The number and severity of these problems increases as birth weight decreases. With the improved survival of more infants who were born too soon or too small comes increased numbers of children born with severe brain damage. The occurrence of cerebral palsy and other forms of brain injury is highly correlated with birth weight. Rates of brain injury total approximately 7% for moderately low birth weight infants (infants weighing between 1,500 and 2,500 grams [3 pounds, 5 ounces and 5 pounds, 8

ounces]) and increases to 20% among the smallest infants (infants weighing between 500 and 1,500 grams [1 pound, 2 ounces and 3 pounds, 5 ounces]). Hack, Klein, and Taylor also note that being born low birth weight is considered an index of biological risk because infants born low birth weight are more likely to have brain damage and/or lung and liver disease.

At school age, children who were born low birth weight are more likely than children of normal birth weight to have mild learning disabilities, attention disorders, developmental impairments, and breathing problems such as asthma.⁴ Children born very low birth weight have more learning problems and lower levels of achievement in reading, spelling, and math than moderately low birth weight children. These problems are reflected in much higher proportions of low birth weight children than normal birth weight children who are enrolled in special education programs (see the article by Hack, Klein, and Taylor). Approximately one-half of all very low birth weight children enroll in special education programs. The adverse consequences of being born low birth weight are still apparent in adoles-

Low birth weight infants have higher rates of subnormal growth, adverse health conditions, and developmental problems.

cence, and experts believe that these abnormalities will be lifelong and will not improve as the children enter adulthood. It must be emphasized that not all of these adverse consequences can be attributed solely to being born low birth weight. Some of the less severe but more common developmental and physical delays reflect the fact that low birth weight children are disproportionately more likely to come from disadvantaged environments. However, it has not been possible to separate the developmental and physical effects of a disadvantaged environment from the effects of being born low birth weight.

Some of the devastating effects of being born low birth weight can be reversed. Hack, Klein, and Taylor discuss how intensive enrichment programs which provide medical and educational services and support for both the parents and the child

have been shown to improve short-term developmental outcomes for low birth weight children. Federal laws mandate that services for school-age disabled children (which include medical, educational, psychological, occupational and physical therapy, and other care) be expanded to include family-based care for infants. At present, these services are targeted to children born with severe congenital disabilities. The availability of services for moderately low birth weight children who do not have severe physical or biological problems varies from state to state, but for the most part, these services are not widely available.

It is not clear what the future holds for tiny infants who only five years ago would not have survived. Initial indications are that a fraction of these very small infants may not fare well and will require substan-

smoking during pregnancy, low maternal weight gain, and low prepregnancy weight. These three risk factors account for nearly two-thirds of all growth-retarded infants.⁵ Other risk factors for low birth weight include black race, first births, female sex, short maternal stature, maternal low birth weight, prior low birth weight birth, maternal illnesses, fetal infections, and a variety of metabolic and genetic disorders. While these risk factors may provide important clues about the causes of low birth weight, many of them are only weakly related to low birth weight and are generally not modifiable by intervention programs or changes in public policy. Even less is known about the risk factors for early delivery. While there are several known risk factors (cigarette smoking during pregnancy, prior preterm birth, low prepregnancy weight, maternal exposure to diethylstilbestrol [DES]), they account for fewer than one-quarter of preterm births.⁵

Translating the current epidemiologic knowledge about the causes of low birth weight and preterm birth into practical preventive care has been difficult and slow. Despite clear and convincing evidence that smoking cessation during pregnancy can prevent growth retardation and low birth weight, intensive smoking cessation interventions are not a routine part of most prenatal care programs. Nutritional interventions do not have as strong or clear an impact on low birth weight as smoking cessation. Even if effective ways could be found to prevent low prepregnancy weight and to promote adequate weight gain, these interventions would help only the small subset of women who are severely undernourished.

One of the more important clues about the causes of low birth weight and preterm birth comes from the observation that there are large ethnic group differences in these outcomes. African-American infants are two times more likely to be born low birth weight or preterm than are white or Asian-American infants. Epidemiologic research has shown that these ethnic group differences are not wholly explained by ethnic differences in the occurrence of various medical conditions, in smoking or use of other licit or illicit drugs, or in use of prenatal care, or by demographic characteristics and other lifestyle differences. Research to discover the reasons for these curious ethnic group differences may shed some light on the causes

Cigarette smoking during pregnancy, low maternal weight gain, and low prepregnancy weight account for nearly two-thirds of all growth-retarded infants.

tial commitments from their families, the medical care system, the educational system, and society in general.

While medical care and technology have gone a long way toward improving the survival of low birth weight infants, preventing the occurrence of low birth weight or preterm birth would be much more advantageous. The next section takes a realistic look at how and if low birth weight can be prevented.

Preventing Low Birth Weight

The Causes of Low Birth Weight and Preterm Birth

To prevent low birth weight and preterm birth, it is necessary to know what causes them and to determine the modifiable factors that are highly related to these causes. Alexander and Korenbrot emphasize that very little is known about the causes of low birth weight and preterm birth despite an extensive amount of research. Low birth weight that results from suboptimal intrauterine growth is associated with three major risk factors: cigarette

of low birth weight and preterm birth as well.

Medical care has been very successful in rescuing the low birth weight infant. However, much less progress has been made in finding solutions to prevent preterm labor or low birth weight. It is logical to think that monitoring the course of pregnancy by providing prenatal medical care might be one means of prevention.

Prenatal Care

Several national commissions have convened experts from many disciplines to determine how to prevent low birth weight and infant mortality.⁶⁻⁸ These commissions have focused on one promising area—prenatal care. Prenatal care varies tremendously but usually includes a package of medical care services in a defined schedule of visits. In addition to medical care, prenatal care programs often include comprehensive educational, social, and nutritional services. While the structure and content of prenatal care was not developed primarily to prevent low birth weight, some data indicate that women who receive prenatal care have fewer low birth weight babies and lower infant mortality. The effectiveness of prenatal care and its components has not been adequately evaluated, and the benefits of this form of care have not been fully measured.⁹ Experimental studies have not been done primarily because it is not ethical to make random assignments of pregnant women to a control group that does *not* receive any prenatal care.

Recent analyses by Alexander and Korenbrot in this issue cast doubt on the degree to which prenatal care is truly effective in preventing low birth weight; self-selection may have produced the apparent advantage. Women who receive prenatal care are a heterogeneous group, but are generally healthier, more educated, and more advantaged than women who do not receive prenatal care. It is unclear whether or not the observed decreased rates of low birth weight among women who receive prenatal care are due to the effectiveness of prenatal care in preventing low birth weight or are due to other differences between women who receive prenatal care and those who do not. Rather than preventing low birth weight, prenatal care may be another indication of the many health-enhancing behaviors that characterize healthy, insured women who have healthy children. Although prenatal care

provides a variety of valuable medical services to pregnant women and fetuses (for example, management of normal birthing, maternal hypertension, and diabetes in the mother and/or detection of congenital malformations and genetic diseases in the fetus) evidence suggests that prenatal care may not provide significant benefits with respect to low birth weight and preterm birth.

Nationally, there has been an increase in the receipt of early prenatal care in the past 20 years. In 1975, 72% of women started prenatal care in the first trimester of pregnancy.⁷ This number rose to 76% in 1980, remained stable throughout the 1980s, and increased to 78% in 1992.^{7,10} Even more notable is that over 98% of all pregnant women currently receive some form of prenatal care.¹⁰ If use of prenatal care actually did prevent low birth weight, then one would expect a decrease in low birth weight with increasing use of prenatal care over time. Population statistics do not confirm this relationship, but these statistics may not tell the entire story because changes in the underlying risk of the population may have obscured the effect of prenatal care on overall rates of low birth weight. International comparisons also raise questions about the ability of prenatal care to reduce rates of low birth weight. American women are more likely than either German or Japanese women to start prenatal care in the first trimester,

Little is done during the standard prenatal care visits that could be expected to reduce low birth weight.

but rates of low birth weight and infant mortality are higher in the United States than they are in either Germany or Japan.

Alexander and Korenbrot also note that recent analyses indicate little is done during the standard prenatal care visits that could be expected to reduce low birth weight. For prenatal care programs to be effective in reducing low birth weight, these programs must target the known causes of low birth weight. Instead, most prenatal care programs are designed to detect major complications of pregnancy, not to prevent low birth weight. These programs start too late to address the prob-

lem of low prepregnancy weight, and few of them include intensive efforts to encourage pregnant women to stop smoking. New analyses also conclude that the often-cited economic benefits of prenatal care, which indicated that, for each dollar spent on prenatal care, direct medical costs savings of up to \$3.38 would be realized, may be overstated.¹¹ In these calculations, the benefits were derived from the expected reductions in hospital stays and intensive care required for low birth weight infants. However, these benefits do not accrue if prenatal care does not significantly prevent low birth weight births. One innovative effort to provide an enhanced form of prenatal care¹² and other efforts to provide intensive interventions to prevent the onset of preterm labor have largely failed to demonstrate reductions in low birth weight.¹³

Prenatal care is a package of necessary services, and a number of benefits accrue from the receipt of these services which do not relate to the prevention of low birth weight. Prenatal care is often an adult woman's first contact with the medical care system, and the screening she receives may uncover manageable conditions

The Medicaid program brought federally funded prenatal and pediatric care to millions of impoverished pregnant women and their children.

and/or treatable diseases which could affect both the baby's life and her own. The education a woman receives about the pregnancy, labor and delivery, and caring for the newborn is very important, particularly for first-time mothers. Prenatal care is also valuable for women who are impoverished because it links them with other valuable social services. The legacy of prenatal care continues after the birth of a child because women who receive this care are more likely to get preventive care for their infants.¹⁴ Moreover, prenatal care may have other positive outcomes which are underassessed. All of these outcomes and others that are as yet unmeasured have potential economic benefits. Thus, the previously cited \$3.38 savings for each dollar spent on prenatal care needs to be reassessed.

Social Programs

Hughes and Simpson discuss how the strong association between socioeconomic status and health problems in children (for example, low birth weight, infectious diseases, asthma, failure to thrive, teenage pregnancy, and child abuse) has resulted in the development of social programs aimed at reducing poverty and its devastating effects. While it is not clear how the mother's socioeconomic status translates into the birth of a low birth weight infant, it is thought that poverty with its associated reduced access to health care, poor nutrition, lower educational levels, inadequate housing, greater physical and psychological stress, and fewer life satisfactions may be responsible for some of the increased risk for low birth weight. In the United States, these programs have focused mainly on improving access to health and medical care for pregnant women, and on temporarily reducing the effects of poverty. However, it is not clear if these programs have had an important impact on low birth weight. Certainly these social programs were developed to ease the effects of poverty on children; in this they succeed. They should not be judged by their uncertain impact on low birth weight.

Hughes and Simpson describe how the introduction of the Medicaid program in 1965 and subsequent eligibility expansions in the 1980s brought federally funded prenatal and pediatric care to millions of impoverished pregnant women and their children. Reductions in low birth weight were found for women who were newly covered by the Medicaid program, but later expansions of eligibility to less severely socioeconomically deprived women were not associated with decreased rates of low birth weight. However, it is not clear how the provision of health care insurance even to women at highest risk translates into reductions in low birth weight, particularly since prenatal care appears to have only a small effect on reducing rates of low birth weight.

Other federal programs aimed at reducing the effects of poverty have also been implemented. The Special Supplemental Food Program for Women, Infants and Children (WIC) provides pregnant women with food vouchers, nutritional education, and referrals to other health and social services. The effects of the WIC program on reducing low birth weight births have been extensively evaluated, and the results have been mixed. Income

supports for impoverished pregnant women became available with the start of the Aid to Families with Dependent Children (AFDC) program in 1935. The AFDC program, more commonly called welfare, is not nearly as well studied as the WIC program. There is some indication that the receipt of welfare is helpful in improving maternal weight gain during pregnancy, but there is little direct evidence to show any relationship between income supports obtained as part of welfare and reductions in low birth weight or preterm births.

Government-sponsored social programs for impoverished families were not designed to reduce rates of low birth weight or infant mortality, but to reduce the financial barriers to medical care for pregnant women and children, and some of the devastating effects of poverty. Therefore, it is not surprising to find that solutions designed to eliminate extreme poverty have made little impact on reducing national rates of low birth weight. The key to preventing this major public health problem does not appear to lie solely in socioeconomic solutions. However, finding ways to prevent low birth weight will probably require discovering reasons for the large variations in birth outcomes by socioeconomic status.

Lifestyle

There are lifestyle choices a woman can make to increase her chances of having a healthy normal birth weight child. Chomitz, Cheung, and Lieberman discuss the role that individual behaviors such as cigarette smoking, use of other drugs, and diet play in determining fetal growth. While women do make their own choices with regard to individual behaviors and overall lifestyles, they also face systemic, psychosocial, biological, and attitudinal barriers to lifestyle changes. In addition, having a healthful lifestyle may not be a high priority for many women who are more concerned with day-to-day survival. Women who are surrounded by poverty and violence and go without adequate housing, food, or employment may turn to unhealthful lifestyle choices as a means of coping. Chomitz and colleagues emphasize that expecting women simply to change their behavior without support and attention from the health care system, society, and influential people in their lives is unrealistic and fosters the belief that women are solely to blame for their undesirable behaviors.

While there are several things women can do to reduce their chances of having a low birth weight infant, one action stands out above all others—*stop smoking cigarettes*. Cigarette smoking is the single largest modifiable risk factor for low birth weight and infant mortality. It accounts for up to 20% of all low birth weight. Smoking retards fetal growth. On average, babies born to smokers weigh about one-half pound less than babies born to nonsmokers. Women who quit smoking during pregnancy significantly reduce the chances that their baby will be born low birth weight. However, most of these “preventable” low birth weight births would be concentrated among those infants born at or near term, who are moderately low birth weight, whose prognoses are quite good, and whose cost of medical care is moderate. Smoking is also associated with preterm birth, but this association is not nearly as strong as that for low birth weight.

Scientists have known about the consequences of smoking during pregnancy for more than 35 years, but they have made little progress in disseminating effective interventions to help pregnant women quit smoking or to keep young women from becoming addicted. Most health care providers are not trained to offer the specialized intensive services needed to help women stop smoking; most insurers do not cover the cost of smoking cessation interventions; and the programs that do exist do not focus on the smoker who is pregnant. Smoking is not a casual activity

Cigarette smoking is the single largest modifiable risk factor for low birth weight and infant mortality.

that can be easily stopped at will; it is a powerful addiction. The addictive powers of nicotine are illustrated in the results of a survey of drug addicts who reported that quitting cigarettes was much more difficult than quitting illicit drugs and alcohol.¹⁵

Other behaviors, such as diet and the abuse of alcohol and other drugs, while important, do not have nearly the impact on overall rates of low birth weight that cigarette smoking has. Abuse of alcohol and other drugs is associated with low birth weight and preterm birth, but relatively

few pregnant women engage in drug abuse. The recent "epidemic" of cocaine use in the United States did not have a large effect on overall rates of low birth weight or preterm birth and may have been confined to local areas.¹⁶ However, some individual mothers and infants do suffer from the effects of drug abuse. Many women who desire to enter drug treatment programs are turned away because programs for drug-abusing pregnant women are generally unavailable.¹⁷

The situation is similar for diet. Because very few women in the United States are severely undernourished, only a small subset of women might be helped by dietary interventions. In addition, little impact on overall rates of low birth weight can be expected by reductions in the number of women having inadequate weight gain during pregnancy, low prepregnancy weight, and abuse of alcohol and other drugs during pregnancy. However, individual women can benefit greatly by abstaining from using drugs during pregnancy and by paying careful attention to their nutritional needs before and during pregnancy. Prenatal care can play an important role in assisting women to maintain healthful lifestyles.

Recommendations

What should and could be done to reduce the problem of low birth weight and infant mortality in the United States? Are there areas of current research and practice that should receive less attention? Are there areas that need to be given higher priority? In the following section, several important steps that could be taken to reduce the number of low birth weight and preterm births in the United States are discussed.

Preventing Low Birth Weight and Preterm Births

Smoking During Pregnancy

The most obvious way to decrease rates of low birth weight and preterm birth is to stop cigarette smoking during pregnancy. Cigarette smoking during pregnancy causes close to one-fifth of all low birth weight births and is the single most important known cause of low birth weight.

■ *Focus additional resources on stopping cigarette smoking during pregnancy.* Because of the highly addictive nature of nicotine, preventing young women from starting to smoke cigarettes should be a high priority. This will require a multilevel commitment

from society, schools, medical care systems, insurers, families, and individuals.

Because cigarette smoking is not likely to be totally abandoned in our society, additional resources should be applied toward helping women quit smoking during pregnancy. These resources need to be allocated to two related areas: developing more effective ways to help pregnant women quit smoking and determining where and how best to implement these interventions. Because nicotine is such an addictive drug, the success rates of most smoking cessation intervention programs are low. Only 9% to 27% of women who participate in these programs are able to quit smoking during pregnancy, and an additional 17% to 28% reduce the amount smoked (see the article by Alexander and Korenbrot). Moreover, many women who do quit during pregnancy relapse quickly after the birth of the baby.¹⁸ The nicotine patch or gum, one of the more effective ways to help smokers quit, is not recommended for use during pregnancy.¹⁸ Thus, to make a measurable impact on reducing rates of low birth weight, new and innovative ways to help pregnant women quit smoking are urgently needed.

Developing ways to integrate smoking cessation interventions into prenatal care seems a logical first step because most pregnant women have contact with health care providers during this period. However simple this appears, it will not be easy, as very few health care providers are prepared to offer such specialized care. Training in smoking cessation should be an integral part of the education of physicians and other reproductive health workers. The effectiveness of utilizing other, non-medical providers to institute smoking cessation programs for pregnant women within the prenatal care setting and elsewhere should be evaluated. These smoking cessation services ideally should be closely linked with prenatal care but need not rely on medical care providers to administer them.

■ *Making sure smoking cessation programs are part of every health insurance package would provide the economic means to pay for these smoking cessation activities.* Studies of the cost-effectiveness of smoking cessation interventions in pregnancy show that relatively small investments in these interventions can have benefits.¹⁹ Costs for smoking cessation interventions may easily be recovered by reductions in medical costs of caring for low birth weight in-

fants¹⁹ and in the need for chronic care for both mother and child in later life.

Prenatal Care

■ *Recognize that for all the valuable contributions prenatal care makes to maternal and child health, in its present form it does little to prevent low birth weight or preterm birth.* From a medical perspective, the purpose of prenatal care is to diagnose and treat a variety of medical conditions that affect the mother and fetus. The medical conditions uncovered during prenatal care affect only a relatively small proportion of all pregnant women and many of these conditions, while important, do not cause low birth weight. However, this should not be interpreted to mean that prenatal care has no value. Prenatal care provides a number of benefits which do not relate directly to the prevention of low birth weight. These include prevention of maternal deaths; education regarding pregnancy, labor and delivery and newborn care; the potential for linking disadvantaged women to important social services; and an increased likelihood that newborns will receive needed preventive care. These and other positive outcomes must be considered in any complete evaluation of prenatal care. However, even the best prenatal care alone cannot be expected to solve the dual problems of low birth weight and preterm birth.

■ *Concentrate resources on improving the content and structure of prenatal and obstetric care.* Prenatal care is an important well-used set of services; not enough, however, is known about the effectiveness of the various components of that care. The content of prenatal care visits is highly variable, and little is known about how well that content corresponds to the needs of pregnant women. Members of a national panel agree that, at a minimum, quality prenatal care should include early and continuing risk assessment, health promotion, and medical and psychosocial interventions and follow-up. The content of prenatal care visits should vary depending on the risk status of the pregnant woman and her fetus.⁹ It is thought that quality care could be provided in fewer prenatal visits, and the schedule of visits should be rearranged so that more visits occur early in the pregnancy and fewer visits occur in the third trimester. The timing of visits should be flexible, and the various aspects of care should be integrated to minimize the number of visits by the woman and the amount of inconvenience to her.⁹ If prenatal care is also to be used as a vehicle for the pre-

vention of low birth weight and preterm birth, care as practiced today needs to be wholly reexamined and restructured to emphasize those elements that can realistically be expected to have a positive impact. In addition, access to prenatal care, while good, is not universal. Improvements in the availability and accessibility of prenatal care are needed, particularly for women who are impoverished or are from disadvantaged groups.⁹

■ *Develop a concerted program of women's health that includes prepregnancy counseling.* Women's health programs that include prepregnancy care should be developed to educate women who are considering pregnancy about things they should do before becoming pregnant. For example, prepregnancy care has the potential to prevent the occurrence of a serious but rare birth defect, spina bifida, which sometimes is caused by extreme dietary deficiencies in folic acid. This is possible only if women are aware of the risk, are screened for diets deficient in folic acid, and if found deficient, are encouraged to take appropriate dietary supplements to assure that they have an adequate intake of folic acid. This intervention will work only if supplements are taken around the time of conception and in early pregnancy. In addition, assuring that women are immune to rubella, controlling the effects of diabetes, and treating sexually transmitted diseases should be done before pregnancy. Because conventional prenatal care is initiated several months after conception, it is not designed to address these and other events that occur before or very early in pregnancy.

■ *Encourage obstetricians to make wider and more frequent use of prenatal corticosteroid treatment.* Each year a sizable number of women have preterm births, and most could benefit from prenatal corticosteroid treatment. While corticosteroid treatment does not actually prevent preterm birth, it has the potential to reduce serious lung disease and brain damage, and to improve the chances for survival among preterm infants.²⁰ Despite very convincing evidence supporting the effectiveness of this treatment, it is currently being offered to only a small minority of the pregnant women who should be receiving it. The infrequent use of such an important therapy brings into question the ability of the medical profession to reach individual physicians with the most current, effective therapies.

Research Needs

Two important areas of research—basic science research and medical and epidemiologic research—will provide the information needed to understand the process of labor and delivery and the causes of low birth weight and preterm birth and will make it possible to prevent these adverse outcomes. The problem of low birth weight is a serious one and has an important economic component. According to Lewit, Baker, Corman, and Shiono, the annual estimated costs of low birth weight (\$6 billion adjusted to 1988 dollars) are more than two times that of AIDS among persons of all ages (\$2.4 billion adjusted to 1988 dollars). Yet, low birth weight receives much less attention and fewer research dollars than AIDS.

■ *Basic Science Research*

■ *Focus additional resources on finding out what triggers preterm labor.* Being born too soon is the main cause of low birth weight and infant mortality in the United States. Finding out what causes preterm labor and the factors that trigger this process will provide the basic knowledge needed to develop and test new ways to prevent preterm birth. At present, there are few clues to guide the search for causes of preterm labor. Nathanielsz notes in his article that, in normal pregnancies, the fetus determines the duration of the pregnancy, and this duration is linked very closely to the maturation of the fetus's vital organs. The initiation of labor also appears to be controlled by the fetus. Specific hormonal changes in the fetus cause the mother's body to produce the signals that initiate labor. Determining the mechanisms for even one of the many critical points in this complex process of labor may make it possible to develop preventive therapies and drugs that could interrupt the process of preterm labor.

The observations by Nathanielsz that the birthing process is a complex multifactorial system of interconnected physiological mechanisms and that preparatory changes occur in the fetus and mother several weeks before labor begins suggest the need to concentrate on the study of preterm labor early in the pregnancy. The effect of infectious agents on the placenta and other parts of the reproductive system also needs to be investigated. Initial studies have shown a connection between infections and preterm labor, but how and if these infections actually initiate the process of labor in humans is not known.

Efforts to find drugs that will suppress or delay preterm labor are ongoing. Currently, drugs to prevent preterm labor are only effective in delaying birth for one to two days; however, several promising new therapies are being tested. Moreover, because the fetus plays a key role in determining the initiation of labor, research on the initiation of labor in humans needs to take a more intensive look at the fetus, particularly the fetal brain and fetal development, to understand the labor process.

■ *Epidemiologic and Medical Research*

■ *Focus resources on discovering the causes of the differences in the rates of preterm birth and low birth weight among racial and ethnic groups.* One of the most important clues about the cause of preterm birth and low birth weight comes from the observation that there are large racial and ethnic group differences in these outcomes. African-American infants are twice as likely as infants of nearly all other ethnic/racial groups in America to be born low birth weight and to be born preterm. Discovering the reasons for these racial differences may provide clues to the causes of preterm birth and low birth weight.

Research in the past decade has not uncovered the reasons for these large ethnic group differences in low birth weight.²¹⁻²⁴ This work has examined the effects of a number of behavioral, socioeconomic, or medical risk factors such as smoking, drug use, inadequate use of medical care, poor health conditions, infections, poverty, employment, physical exertion, poor nutrition, stress, and lack of social support. Interestingly, Hispanic and Asian-American women who have similar levels of poverty to African Americans have rates of low birth weight and infant mortality comparable to white infants. This provides some evidence that poverty may not be the sole reason for the high rates of infant mortality among African Americans.²¹ While it is valuable to know what does *not* cause the racial group differences in low birth weight and preterm birth, more emphasis needs to be placed on studying the basic biological differences between the racial groups which may be responsible for these disparities.

Another important observation is that the average birth weights of African-American and Asian-American infants are approximately one-half pound less than those of white infants.²¹ However, in spite of their lower average birth weights, the

rate of infant mortality for Asian-American infants is the same as or lower than the rate for white infants.²⁵ In contrast, African-American infants have average birth weights that are similar to those of Asian-American infants, yet African-American infants are twice as likely to die as either white or Asian-American infants.²⁵ These observations illustrate the apparently normal variations in the birth weight distribution, with two groups—whites and Asian Americans—having very different birth weight distributions, yet similar rates of low birth weight and infant death. This leads to the conclusion that merely having small babies is not the entire problem, but that as-yet unknown factors predispose African Americans to having very small preterm infants who are more likely to die. However, simple measures such as birth weight and gestational age are not enough to explain important ethnic group differences in outcomes.

One area of needed research is the potential biological or genetic differences between the racial and ethnic groups which distinguishes between the low birth weight that occurs as a result of normal variability in infant size and the low birth weight that occurs as a result of environmental and/or biological injury. It appears likely that a disproportionate number of African-American low birth weight births occur as a result of environmental and/or biological injuries, and not as a result of normal variations in infant size. Normal variability in size would not be responsible for the doubled rate of infant mortality, whereas, an increase in the number of low birth weight infants born as a result of these injuries could result in increased rates of infant mortality. However, the degree to which the observed differences in low birth weight and early delivery among the racial or ethnic groups reflects normal biological variation is currently unknown. If social and economic reasons are not the dominant cause of these racial differences, then these observations cry out for biological explanations.

■ *Simultaneously emphasize the role of socioeconomic, environmental, and lifestyle factors along with genetic and physiological factors in future research.* What makes the African-American fetus more likely and the white or Asian-American fetus less likely to initiate preterm labor? The answers to these questions will probably be multifaceted. At the root of the question is the complex interplay of individual susceptibility and

the multitude of potential environmental stimuli. One way to begin to answer this question is to focus more closely on pregnancy and labor among African Americans and to look for physiological differences in these processes which might provide clues about the racial disparities in infant mortality. A clear understanding of why babies are born too early and sick may make it possible to eliminate these ethnic differences in infant mortality.

Caring for Low Birth Weight and Preterm Infants

■ *Develop ways to improve the quality of medical care by assuring that proven, effective technologies are used and disseminated, and that ineffective technologies are abandoned.* The tremendous advances in neonatal intensive care technologies over the past 20 years carry a high price tag. Low birth weight infants make up 7% of all infants, but 35% of the dollars spent on health care for infants goes toward their care, with nearly half of these dollars going toward the care of the tiniest infants. A disturbing majority of specific technologies, procedures, and therapies included as part of this intensive care have never been adequately tested for their effectiveness.

Because of the high cost and experimental nature of many neonatal intensive care technologies and therapies, it is crucial that the evaluation of these technologies and therapies receive particular attention. It is especially important to study the subset of extremely tiny infants who are now surviving as a result of this intensive care. Tyson makes the point that many, if not most, of the interventions practiced as part of neonatal intensive care have not been formally evaluated in clinical trials. Clinical trials should be set up on a national basis which would allow the families of these tiny newborns the opportunity to join ongoing studies. Perhaps study of the efficacy of neonatal intensive care could be modeled after the Children's Cancer Group and the Pediatric Oncology Group, which enroll the vast majority of children diagnosed with cancer into randomized trials that test the efficacy of different forms of treatment for these rare conditions. In this way, the care of these infants could be studied, and the valuable information about their care and treatment is used to improve future care. Information about the long-term consequences of these intensive care procedures should also be combined with data on the cost of caring for these infants.

Promoting only those technologies that are proven to be effective and abandoning those that are ineffective will conserve health care dollars and keep infants from receiving unnecessary, often invasive procedures.

Clinical evaluation science is a new and growing field which could provide the infrastructure to help improve the quality of medical care for women and children. Techniques such as meta-analysis, in which evidence from several clinical trials is objectively synthesized, are being used to develop practice guidelines which provide clinicians with current information about how to care for particular illnesses. In addition to helping physicians decide how to treat particular conditions, clinical evaluation science takes the next very important step and concentrates on developing more effective ways to help physicians actually change the way they practice medicine. The goal of clinical evaluation science is to rely on data-driven solutions rather than on chance occurrences to direct the practice of medicine. To make this form of quality improvement work requires a team approach among health care providers, insurers, and consumers.

■ *Define what care, if any, should be given to the most immature, malformed, or sick infants.* While future research will further define the effectiveness of the specific technologies used as part of neonatal intensive care, resources need to be focused on how to decide which infants should be administered intensive care and which infants should be treated with "comfort care." Without intensive care, most of the very small, sick infants will die soon after birth. However, while intensive care may have the power to save some of these infants, it also has the power to prolong the pain, the suffering, and the process of dying for many others. Federal child abuse laws require the use of intensive care for all critically ill infants, except when the care is futile or inhumane. However, the interpretation and application of this law has been inconsistent because the law as written provides very little practical guidance for clinicians and families on how to determine if care is futile or inhumane. Practical guidelines are needed to help families and physicians make decisions regarding the care of critically ill infants whose chances for survival are poor. These guidelines should assure that the interests of the infant, the parents, health care providers, and society are represented without creat-

ing a bureaucracy that interferes with the patient-physician relationship.

■ *Increase support for programs to define new and better ways to meet the wants and needs of distraught parents who are likely to be faced with the birth of a critically ill baby.* Strategies should be developed to help assure that parents are informed about the condition of their infant, the treatment options, and the future prospects for their child's development. Ideally, discussions should occur between the parents and health care providers before the birth of an affected child so that parents are able to make these very difficult decisions outside a crisis situation. The potential for creating undue concern among parents must be balanced with the desirability of having them be fully informed about the numerous but extremely rare potential adverse outcomes. The role of parents, medical care providers, researchers, policymakers, and society in the process of making crucial decisions about the care of these extremely fragile and tiny infants also needs to be clarified.

■ *Maintain a constant and ongoing commitment to children who are born low birth weight or preterm.* Commitment to these children should not stop when they go home from the hospital. Most low birth weight and preterm infants grow up to be healthy adults. However, some low birth weight infants are not so lucky. These infants—particularly the extremely low birth weight infants and their families—must learn to cope with challenging lifelong disabilities. Data show that the adverse health and developmental effects of being born low birth weight can often be reversed. Federal laws also mandate services for disabled children, including those with disabilities resulting from being born low birth weight. Additional resources should be provided to assure that these disabled children receive the health, educational, psychological, and social services they need.

In the current wave of deregionalization, neonatal intensive care for critically ill newborns appears to be moving from centralized university-based settings to more diffuse suburban settings. As part of regionalization of care, multiservice follow-up clinics were also strategically placed at university-based hospitals which had the capacity to serve a large regionalized population and staff these centers with the necessary highly trained medical and developmental specialists. These multiservice clinics have made it possible for families with children who have serious medical

and developmental problems to receive high-quality coordinated care in an efficient way. Whether diffusion of intensive care will enhance access to existing regionalized centers or inadvertently introduce new barriers for families of very ill children who need follow-up services after they leave the hospital is unclear. Local action may be required to assure that needed services are available to these children.

Conclusion

Public health measures such as population rates of low birth weight, preterm birth, and infant mortality are important indicators of the status of a nation's health. On a population level, these measures provide an objective overview of the ability to apply specific knowledge of the basic sciences, medical care, social programs, and the consequences of lifestyle behaviors in preventing these undesirable outcomes. Charting rates of low birth weight and other population measures over time also provides an indication of how national policy should be directed.

Implementing social and medical programs that are specifically targeted to improve these public health measures makes good sense, particularly when they are designed using existing unbiased knowledge about the causes of the problem and how to implement such preventive programs effectively. However, benefits should not be attributed where none exist. Expecting social programs such as Aid to Families with Dependent Children, WIC, and Medicaid, and medical care programs such as prenatal care to reduce national rates of low birth weight, preterm birth, and infant mortality significantly is unwarranted, particularly since these programs were not specifically designed to impact these pub-

lic health measures. Public health advocates need to be wary of exaggerating the claims of such programs and not be tempted to ascribe positive outcomes where none exist.

Alternatively, these established medical and social programs should not be abandoned merely because they do not impact on population public health measures. Taking such a narrow view of the benefits of these social and medical programs severely underestimates their potential benefits. Further, the benefits of medical care provided to an individual clearly exist even though changes in general population statistics cannot be demonstrated. It is particularly crucial, in the current political and economic climate which is focused on finding ways to decrease government involvement, not to be tempted to abandon important programs based on a very narrow view of efficacy.

If policy directions are to be guided by current knowledge about preventing the major cause of infant mortality, low birth weight, and preterm birth, then the focus must be on those practices and technologies that clearly are effective. While there is an urgent need to know more about the physiological mechanisms that trigger preterm birth, produce growth retardation, and heighten the risk of infant mortality, there is no need to wait for major breakthroughs in these areas to reduce the number of infants born low birth weight. Several proven means exist to prevent these tragic birth outcomes, and they should be fully utilized now.

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Richard E. Behrman

1. Standard terms are used to describe the weight and age of newborns. These terms are also used to indicate potential risk for these newborns. These terms are *low birth weight* and *preterm*.
Low birth weight (LBW) = under 5 pounds, 8 ounces, or 2,500 grams
Very low birth weight (VLBW) = under 3 pounds, 5 ounces, or 1,500 grams
Extremely low birth weight (ELBW) = under 2 pounds, 3 ounces, or 1,000 grams
Preterm birth = birth after fewer than 37 weeks of gestation
Very preterm birth = birth after fewer than 32 weeks of gestation
2. Wegman, M.E. Annual summary of vital statistics—1993. *Pediatrics* (1994) 94:792–803.
3. Allen, M.C., Donohue, P.K., and Dusman, A.E. The limit of viability—Neonatal outcome of infants born at 22 to 25 weeks' gestation. *New England Journal of Medicine* (1993) 329:1597–1601.
4. Hack, M., Taylor, G., Klein, N., et al. School-age outcomes in children with birth weights under 750 g. *New England Journal of Medicine* (1994) 331:753–59.

5. Kramer, M.S. Determinants of low birth weight: Methodological assessment and meta-analysis. *Bulletin of the World Health Organization* (1987) 65:663–737.
6. Institute of Medicine, Committee to Study the Prevention of Low Birth Weight. *Preventing low birth weight*. Washington, DC: National Academy Press, 1985.
7. Institute of Medicine, Committee to Study Outreach for Prenatal Care. *Prenatal care: Reaching mothers, reaching infants*. Washington, DC: National Academy Press, 1988.
8. National Commission to Prevent Infant Mortality. *Death before life: The tragedy of infant mortality*. Washington, DC: NCPIM, 1988.
9. U.S. Department of Health and Human Services, Public Health Service Expert Panel on the Content of Prenatal Care. *Caring for our future: The content of prenatal care*. Washington, DC: DHHS, 1989.
10. National Center for Health Statistics. *Advance report of final natality statistics, 1992*. Monthly Vital Statistics Report, Vol. 43, No. 5, Suppl. Hyattsville, MD: Public Health Service, 1994.
11. Huntington, J., and Connell, F.A. For every dollar spent—The cost-savings argument for prenatal care. *New England Journal of Medicine* (1994) 331:1303–7.
12. Korenbrot, C., Clayson, Z., Gill, A., and Patterson, E. *Evaluation of the implementation of the Comprehensive Perinatal Service Program. Final report*. San Francisco: Institute for Health Policy Studies, University of California, 1993.
13. Collaborative Group on Preterm Birth Prevention. Multicenter randomized, controlled trial of a preterm birth prevention program. *American Journal of Obstetrics and Gynecology* (1993) 169:362–66.
14. Bates, A.S., Fitzgerald, J.F., Dittus, R.S., and Wolinsky, F.D. Risk factors for underimmunization in poor urban infants. *Journal of the American Medical Association* (1994) 272:1105–9.
15. Kozlowski, L.T., Wilkinson, D.A., Skinner, W., and Kent, C. Comparing tobacco cigarette dependence with other drug dependencies. *Journal of the American Medical Society* (1989) 261:898–901.
16. Shiono, P.H., Klebanoff, M.A., Nugent, R.P., et al. The impact of cocaine and marijuana use on low birth weight and preterm birth: A multicenter study. *American Journal of Obstetrics and Gynecology*. (1995) 172:19–27.
17. Kumpfer, K. Treatment programs for drug-abusing women. *The Future of Children* (Spring 1991) 1,1:50–60.
18. Samet, J.M., Lewit, E.M., and Warner, K.E. Involuntary smoking and children's health. *The Future of Children* (Winter 1994) 4,3:94–114.
19. Marks, J.S., Koplan, J.P., Hogue, C.J.R., and Dalmat, M.E. A cost-benefit/cost-effectiveness analysis of smoking cessation for pregnant women. *American Journal of Preventive Medicine* (1990) 6:282–89.
20. Effect of corticosteroids for fetal maturation on perinatal outcomes. NIH Consensus Statement 1994, February 28–March 2; 12,2:1–24.
21. Shiono, P.H., Klebanoff, M.A., Graubard, B., et al. Birth weight among women of different ethnic groups. *Journal of the American Medical Association* (1986) 255:48–52.
22. Kleinman, J., and Kessel, S. Racial differences in low birth weight. *New England Journal of Medicine* (1987) 317:749–53.
23. Shiono, P.H., and Klebanoff, M.A. Ethnic differences in preterm and very preterm delivery. *American Journal of Public Health* (1986) 76:1317–21.
24. Shiono, P.H., Rauh, V.A., Park, M., et al. Ethnic differences in birth weight: The role of lifestyle, social, psychological, medical, and other factors. Unpublished manuscript.
25. *March of Dimes statbook: Statistics for healthier mothers and babies*. White Plains, NY: March of Dimes Birth Defects Foundation, 1993.

The Problem of Low Birth Weight

Nigel S. Paneth

Abstract

Low birth weight is a major public health problem in the United States, contributing substantially both to infant mortality and to childhood handicap. The principal determinant of low birth weight in the United States is preterm delivery, a phenomenon of largely unknown etiology. Preterm delivery is more common in the United States than in many other industrialized nations, and is the factor most responsible for the relatively high infant mortality rate in the United States.

Within the United States, Asian populations experience the lowest preterm delivery rates, while Hispanic and Native American populations experience slightly higher preterm delivery rates than the white population. African Americans, however, have much higher rates of preterm delivery than any of the other major ethnic groups. Poverty is strongly and consistently associated with low birth weight, but the precise social and environmental conditions that produce preterm delivery have not been elucidated. Although it is popular to link illicit drug use to low birth weight, a high low birth weight rate was characteristic of the United States for decades before the cocaine epidemic of the 1980s.

Neither the low birth weight rate nor the preterm delivery rate has improved in the United States in the past quarter century. Most efforts to prevent prematurity or low birth weight, when carefully evaluated, have not proven effective. A major goal of biomedical research ought to be better understanding of the causes of this important public health problem.

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Low birth weight is, at once, a public health problem of the first rank and a scientific problem of immense interest. As a public health problem, its high priority stems from the facts that it is the major determinant of infant mortality in developed countries and that it contributes substantially to the overall burden of childhood handicap. Both low birth weight (conventionally defined as less than 2,500 grams, or 5 pounds, 8 ounces) and its major antecedent, preterm delivery (usually referring to birth prior to 37 completed weeks of gestation), are more common in the United States than in most other Western European nations, and these differences account for our nation's relatively poor infant mortality. Moreover, the African-American population in the United States experiences an especially high prevalence of low birth weight and preterm births, which fuels the black-white gap in infant mortality and indicates that equality of opportunity for life is an American ideal unfulfilled even at birth.

At the same time, we must acknowledge that low birth weight is not a simple public health problem. Of the many solutions that have been proposed (often enthusiastically) to remedy this serious disorder, few, if any, have proven effective. In

Low birth weight and/or preterm delivery are factors in most neonatal deaths in the United States.

spite of advances in the medical care of pregnancy and delivery, and the introduction of a variety of programs that have substantially increased the access of impoverished populations to that care, the proportion of births that are low birth weight has changed little in the United States in the past 30 years, and the difference in this index between black and white populations has not lessened. Although medical innovation has played a major role in lowering infant mortality, its impact on the prevalence of low birth weight appears to have been minimal.

Thus, it is not sufficient to assert that low birth weight is a societal problem, solvable, in the present state of knowledge, through the further application of established social and medical programs. Rather, better understanding of the nature of low birth weight and preterm delivery must be made a high scientific priority.

Three principal concerns have focused public attention on the problem of low birth weight. These are

- the impact of low birth weight on infant mortality and subsequent morbidity,
- the social class and ethnic gradients in low birth weight, and
- the relatively high infant mortality rate in the United States.

Low Birth Weight and Infant Mortality and Later Morbidity

In industrialized countries, infant mortality is closer to birth, both in time and in its relationship, than in developing countries. The largely infectious and nutritional diseases that cause 10% or more of infants to die by their first birthday in

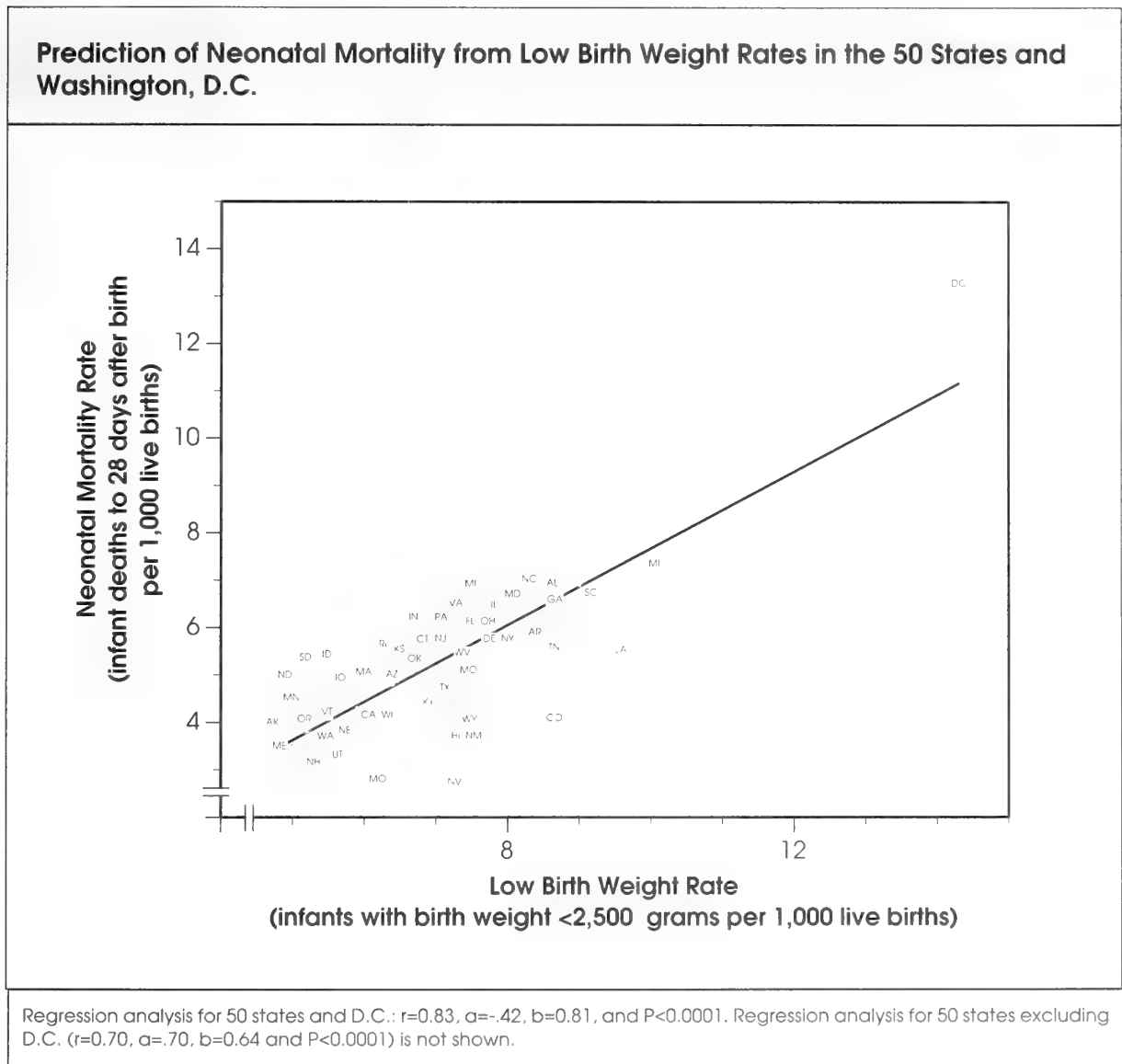
much of the world occur, for the most part, after the immediate neonatal period. Having conquered these causes of infant death in industrialized nations, we now find that the approximately 1% of infants who die in the first year of life most often do so in the first few weeks after birth. Neonatal (first month) mortality accounts for about three-quarters of infant (first-year) mortality in most industrialized countries. Thus, the immediate outcome of pregnancy determines infant mortality in industrialized countries, and the chief indicator of how pregnancy has progressed is the infant's birth weight.

Low birth weight is, in fact, so directly related to neonatal mortality that the relative position of each state's neonatal mortality rate can be predicted with reasonable accuracy from the proportion of low birth weight infants (those weighing less than 2,500 grams, or 5 pounds, 8 ounces, at birth) among live births. (See Figure 1.) An even better prediction can be obtained from the very low birth weight rate (the proportion of births weighing less than 1,500 grams, or 3 pounds, 5 ounces). Unlike infants weighing less than 2,500 grams at birth, very low birth weight infants are virtually always born preterm, and their mortality is considerable even in the presence of intensive care.

Low birth weight and/or preterm delivery are factors in most neonatal deaths in the United States. In New York City between 1976 and 1978, 73.7% of neonatal deaths in white infants and 83.4% of those in black infants occurred in babies who either weighed less than 2,500 grams or were born prior to 37 weeks of gestation.¹

Low birth weight and, especially, very low birth weight infants are also predisposed to a variety of neurodevelopmental disorders and later suboptimal health, a topic reviewed in detail by Maureen Hack and colleagues in this journal issue. The most important of the major handicaps to which low birth weight infants are susceptible is cerebral palsy, found about 25 times more commonly in children who had been very low birth weight infants.² In addition, deafness,³ blindness,⁴ epilepsy,⁵ chronic lung disease,⁶ learning disabilities, and attention deficit disorder⁷ are all found more commonly in low birth weight infants. Moreover, because the incidence of low birth weight is strongly associated with poverty, low birth weight children often suffer the added burdens posed by inadequate environments which interact

Figure 1



Sources: Lee, K., Paneth, N., Gartner, L.M., and Pearlman, M. The very low birth weight rate: Principal predictor of neonatal mortality in industrialized populations. *Journal of Pediatrics* (1980) 97:5759-64; National Center for Health Statistics. Advance report of final natality statistics, 1992. Monthly Vital Statistics Report, Vol. 43, No. 5, Suppl. Hyattsville, MD: Public Health Service, 1994; National Center for Health Statistics. Advance report of final mortality statistics, 1992. Monthly Vital Statistics Report, Vol. 43, No. 6, Suppl. Hyattsville, MD: Public Health Service, 1994.

with biological forces to increase yet further the extent of cognitive and functional disability.

Social Disadvantage and Low Birth Weight

Low birth weight is the central biological mediator of the relationship of social class and economic conditions to infant mortality in industrialized countries. Virtually all of the several indicators of parents' social position (occupation, educational achievement, income, marital status)

which are associated with infant mortality exercise their effect by altering the birth weight distribution.⁸ A detailed review of the nature of these relationships is given by Hughes and Simpson in this journal issue. But by what mechanism is social disadvantage translated into low birth weight?

At first glance, an obvious mechanism is nutrition: poor women might have lower caloric intake which impairs fetal growth and results in low birth weight. However, because caloric restriction (as contrasted to other forms of malnutrition) is not

widespread in the United States, and because caloric supplementation appears to have only a modest effect on birth weight in the United States,⁹ this mechanism would appear to explain little of the social

The social and economic conditions in which preterm delivery and low birth weight thrive are more prevalent in the United States than in other industrialized nations.

gradient of low birth weight in the United States. A more likely mediator is smoking during pregnancy. Smoking exhibits a clear social class gradient in most developed countries with the poorest mothers smoking the most.¹⁰ As noted by Chomitz in this journal issue, smoking has a pronounced effect on fetal growth, and at least some of the social class gradient in low birth weight can therefore be explained by differences in smoking habits.

But neither of these two mechanisms is very strongly linked to preterm delivery, and it is preterm delivery that underlies most low birth weight in the United States. Preterm delivery, like low birth weight, is related to socioeconomic circumstances, but as yet, no mechanism has clearly elucidated the relationship of social class to preterm delivery. Research to develop better understanding of the mechanism or mechanisms by which disadvantaged social circumstances are translated into shortened gestation should be high on the scientific agenda.

International Comparisons of Infant Mortality

The United States ranks 22nd in infant mortality among nations.¹¹ Infant mortality is lower in all five Scandinavian nations, in much of the rest of Western Europe, and in Japan, Singapore, and Hong Kong. If the white population of the United States was considered separately, it would rank no better than 13th in the international comparisons.^{11,12}

These differences are explainable by the higher rate of low birth weight and preterm delivery in the United States. When U.S. and Scandinavian infants of the same birth weight are compared, it is found that mortality is actually lower in the United States.¹³ This mortality pattern in-

dicates that our response to low birth weight has been effective at the level of treatment but not at the level of prevention. At the same time, it indicates that the social and economic conditions, still poorly understood, in which preterm delivery and low birth weight thrive are more prevalent in the United States than in other industrialized nations with similar or even fewer economic resources.

Figure 2 shows that infant mortality parallels the low birth weight rate and the preterm birth rate quite consistently in international comparisons.

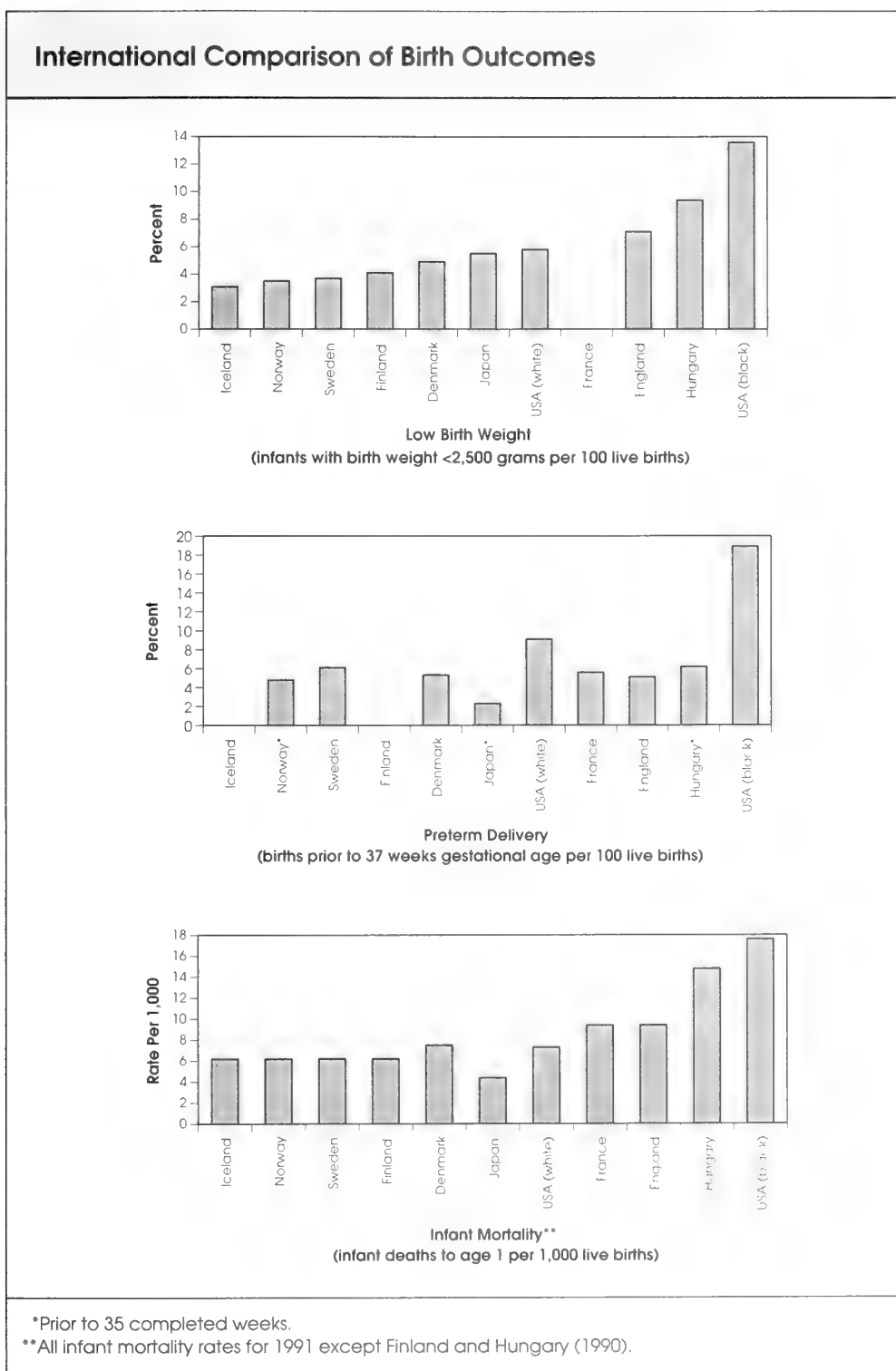
The Scandinavian nations with low infant mortality rates have very low proportions of low birth weight and preterm births, especially in their upper social classes. In Sweden, the socioeconomically most privileged mothers deliver before 37 weeks in only about 4% of their pregnancies,¹⁴ less than half the rate for U.S. whites and less than a quarter the rate for U.S. blacks. Hungary has long been an outlier among European nations for its high infant mortality rate. The Hungarian low birth weight rate of 9.0% is higher than that of most other European nations, and the low birth weight rates for less educated Hungarian women (23.3%)¹⁵ are as high as those found anywhere in the world, including among African Americans in Detroit (25.7%).¹⁶ Thus, in Europe, as in North America, infant mortality reflects quite closely the prevalence of low birth weight and preterm delivery.

A Closer Look at Low Birth Weight

The first step in better understanding any public health problem is developing a language to describe it accurately. Low birth weight at first glance seems to be a simple concept: any baby below a certain threshold of weight is a low birth weight baby. But what threshold? And should it be the same for babies of all types and from all populations? Are there different kinds of low birth weight babies?

The World Health Organization adopted, in 1950, the figure of less than 2,500 grams (or 5 pounds, 8 ounces) as a universal definition of low birth weight, and this figure has been used in most studies of the subject for the decades since.¹⁷ But populations vary considerably in the size of their babies at birth. At one extreme, mean birth weight among in-

Figure 2



Sources: *Proceedings of the international collaborative effort on perinatal and infant mortality*. Vol III. DHHS/PHS 92-1252. Hyattsville, MD: National Center for Health Statistics, 1992; Kohler, L., and Jakobsson, G. *Children's health and well-being in the Nordic countries*. London: Mac Keith, 1987; Berkowitz, G.S., and Papiernik, E. Epidemiology of preterm birth. *Epidemiology Reviews* (1993) 15:414-43; World Health Organization. *World health statistics annual*, 1991. Geneva: WHO, 1993; World Health Organization. *United Nations demographic yearbook*, 1986. Geneva: WHO, 1988; National Center for Health Statistics. *Advance report of final natality statistics, 1991*. Monthly Vital Statistics Report, Vol. 42, No. 3, Suppl. Hyattsville, MD: Public Health Service, 1993; National Center for Health Statistics. *Advance report of final mortality statistics, 1991*. Monthly Vital Statistics Report, Vol. 42, No. 2, Suppl. Hyattsville, MD: Public Health Service, 1993.

fants born in India is about 2,900 grams (6 pounds, 6 ounces); at the other, the average Swedish baby weighs 3,500 grams (7 pounds, 11 ounces). African-American babies weigh on average about 250 grams (9 ounces) less at birth¹⁸ and Asian-American babies, about 150 grams (5 ounces) less,¹⁹ than do white American babies, who, in turn, weigh 100 to 150 grams (4 to 5 ounces) less than Scandinavian babies.

Do these average birth weights reflect the diversity of human biology or the effects of social disadvantage? On the one

the birth weight distribution, and it is noteworthy that birth weight in all sizable populations is not quite normally distributed, but has a larger lower tail than expected, reflecting an excess of small babies. Several mathematically oriented investigators, including Ashford, Brimblecombe, and colleagues^{21,22} and Wilcox and Russell,^{23–25} have argued that the roughly normal birth weight curve in any population is really a mixture of two distributions, one of the normal population and the other of a pathological group of babies (referred to as the “residual” distribution) in whom small size is a reflection of some unhealthy maternal or fetal condition.

But just as it is not easy to tell, without obtaining further information, whether a child small for its age is a healthy small child or has a medical condition interfering with growth, it is not simple to separate these overlapping populations of low birth weight infants. Wilcox and Russell have suggested a method for separating the two and have made an argument that the difference in the United States between African-American and white birth weights is partly due to a lower average birth weight among apparently healthy African-American babies and partly due to an excess of babies with very low birth weight who have a substantial excess risk of mortality.²⁶

Comparing Japanese babies to African-American babies, as was done recently by Kleinman,²⁷ illustrates the value of this distinction. Japanese babies are not particularly large; median birth weight is about the same as that for U.S. blacks, about 3,200 grams (or 7 pounds). But these two populations differ markedly in the proportion of births in the residual distribution, babies who are small for presumably pathological reasons. Kleinman estimated that in Osaka 1.3% of babies were in this distribution, but among U.S. blacks the comparable figure was calculated to be 4.3%. This difference, because it is composed of infants at very high risk of death, profoundly influences the infant mortality rate and explains why mortality is so much higher among African-American infants than among Japanese infants, even though both populations have relatively low mean birth weights. The important point to note is that it is the pathological conditions that lead to an excess of small babies in the residual distribution that should stimulate public health action, not that part of the variation in birth

A baby is small at birth either because it was born too soon, because it grew too slowly in utero, or because of some combination of the two.

hand, we do not wish to ignore threats to human health by suggesting that differences in certain biological parameters are “natural.” But on the other hand, we would be wrong to adopt a standard for anthropometric measurements derived from a population of European origin and claim that it must apply to everyone. One way of reconciling these perspectives is to see if the variation in birth weight among populations can be separated into pathological and nonpathological components.

Within quite a large range of human birth weights and a somewhat narrower range of durations of gestation, infant mortality varies little and makes only a small contribution to the overall infant mortality picture. This variation is exemplified by comparing Indian populations in England to their compatriots of Anglo-Saxon origin. Although mean birth weight is sharply lower (by almost 250 grams, or 9 ounces) in the offspring of Punjabi immigrants, perinatal mortality is not affected.²⁰ This difference in average birth weight appears simply to reflect the genetic diversity of humankind.

Like adult height, variation in birth weight of this sort confers no intrinsic health advantage or disadvantage. But if we choose a universal threshold below which we define low birth weight, we will mistakenly define Indian immigrants as a population with a high incidence of a pathological condition.

Infant mortality is most substantially affected by variation of the lowest tail of

weight which appears to be irrelevant to human health.

For public policy purposes then, a single cutoff for low birth weight in all populations must be treated with a certain amount of skepticism. It is a crude indicator, useful for making a quick and rough assessment, but one that needs more refinement if public policy initiatives are to be appropriately targeted. An ingenious, but mathematically somewhat laborious, method for calculating the ideal low birth weight threshold for each population has been proposed by Chen and colleagues.²⁸ Kleinman, in the paper discussed above, has suggested a simpler method which does not require complex computations.

Size, Weight, and Maturity

Even if we could agree on a way of describing low birth weight that took account of population differences in ordinary non-pathological birth weight, we would still be dealing with a heterogeneous entity because there are several pathways to pathological low birth weight. For many years, low birth weight and prematurity were essentially synonymous concepts. A wise clinician, Arvo Ylppo, recognizing the difficulty of determining the length of gestation, advocated, early in this century, the use of a simple threshold level of 2,500 grams (5 pounds, 8 ounces) to distinguish babies in need of special assistance during the neonatal period. Adopted by the World Health Organization,¹⁷ this pragmatic operational rule for nurseries became established as a population measure and often a substitute for clear biological thinking. For just as the weight of a child does not tell us the child's age (although it can provide a rough approximation), birth weight does not tell us the duration of gestation.

A baby is small at birth either because it was born too soon, because it grew too slowly in utero, or because of some combination of the two. Preterm delivery and fetal growth appear to have distinct determinants, and one of the most important and little-appreciated observations about the state of our knowledge in this area is that, while we have considerable understanding of the causes of impaired fetal growth, we know next to nothing about the causes of preterm delivery.²⁹ To add another wrinkle, even the word prematurity is a misnomer for babies born after too short a period of gestation because babies of the same gestational age may

differ in their level of maturation.³⁰ Preterm delivery is the most accurate term to use in describing babies born too soon in chronological time.

Preterm delivery and impaired fetal growth differ in another important way. The former is much more important as a cause of infant mortality in developed nations.³¹ Fetal growth impairment, though

Preterm delivery is much more important as a cause of infant mortality in developed nations.

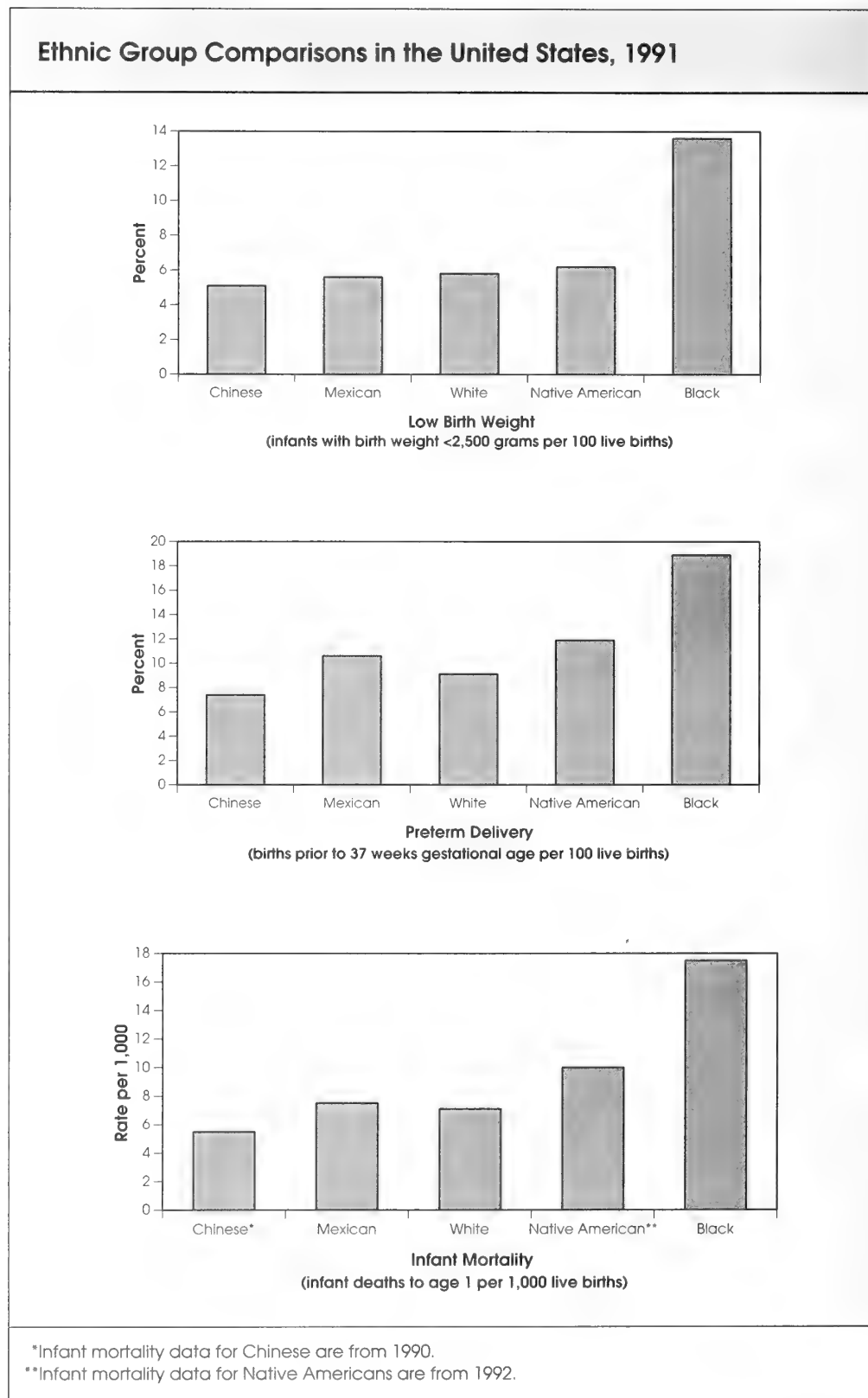
not rare, does not exert the same force of mortality as does early delivery. The long-term impact of fetal growth retardation on neurodevelopment, though more important than its effect on the newborn,³² is also not as pronounced as the effect of preterm birth. Studies of low birth weight as a homogeneous entity have probably seen their day. Gestational age is better assessed in routine obstetric practice than in the past,³³ and the recording of gestational age in vital data has, no doubt, also improved. This offers new opportunities to investigate the causes of preterm delivery, historically overlooked in the great mass of often unfruitful etiologic literature on low birth weight.

The Special Problem of Preterm Delivery and Ethnicity in the United States

In Figure 3, we show, from the most recent data available, the infant mortality rate, preterm delivery rate, and low birth weight rate for several U.S. ethnic groups.

In the United States, in 1991, the median birth weight of white babies was 3,410 grams (7 pounds, 8 ounces), and of black babies, 3,160 grams (6 pounds, 15 ounces), a difference of 250 grams (9 ounces). At the same time, the low birth weight rate was 13.6% among black babies and 5.8% among white babies. Black babies constitute 17% of all births, 33% of all low birth weight births, and 38% of all very low birth weight births in the United States. This high rate of low birth weight is not found among other ethnic minorities in the United States. Hispanic, Native American, and Asian-American populations have low birth weight rates very close to those of American whites.

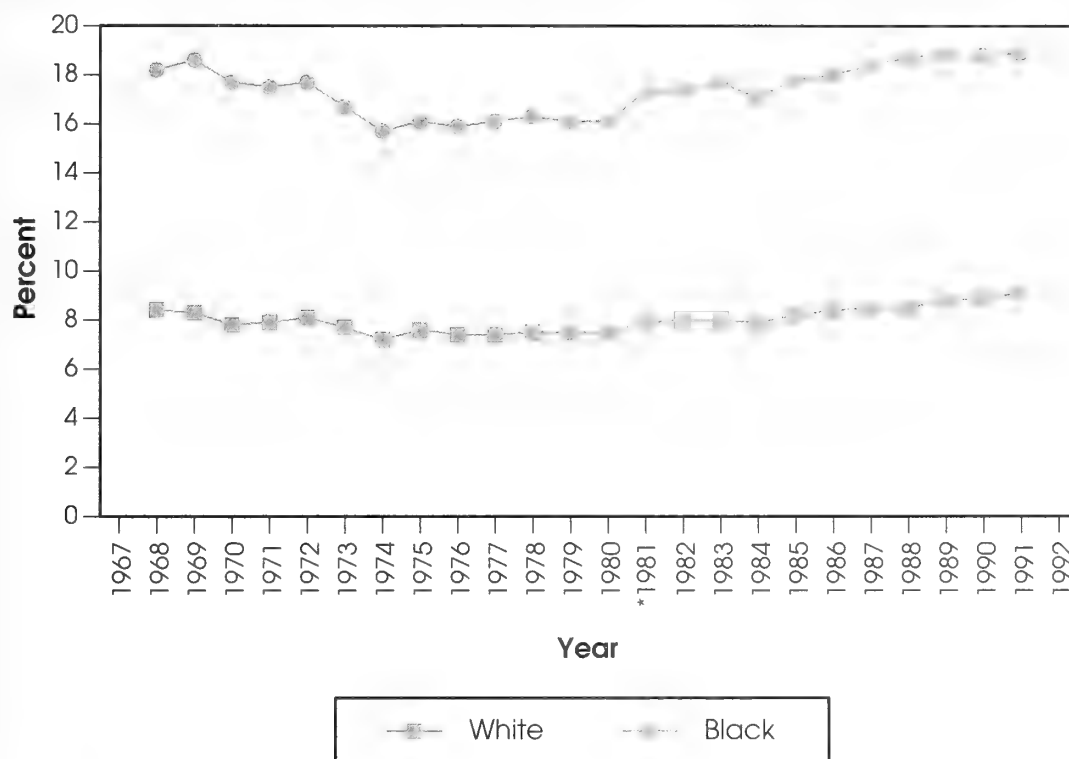
Figure 3



Source: National Center for Health Statistics. *Advance report of final natality statistics, 1991*. Monthly Vital Statistics Report, Vol. 42, No. 3, Suppl. Hyattsville, MD: Public Health Service, 1993; National Center for Health Statistics. *Advance report of final natality statistics, 1992*. Monthly Vital Statistics Report, Vol. 43, No. 5, Suppl. Hyattsville, MD: Public Health Service, 1994; National Center for Health Statistics. *Vital statistics of the United States, 1990*. Vol. II. Washington, DC: U.S. Government Printing Office.

Figure 4

Proportion of Live Births Born Before 37 Completed Weeks of Gestation by Race in the United States, 1968–1991



*The definition of gestational age changed in 1981 when some last menstrual period dates were imputed.

Sources: Paneth, N. Recent trends in preterm delivery rates in the United States. *INSERM Colloque: Prevention of Preterm Birth* (1986) 138:15–30; National Center for Health Statistics. *Advance report of final natality statistics*. Monthly Vital Statistics Report. Hyattsville, MD: Public Health Service. (1968 through 1991.)

Underlying the high rate of low birth weight among African Americans is the strong association of preterm delivery and race. Black infants are more than twice as likely as white infants in the United States to be born prior to 37 weeks of gestation (Figure 4). Moreover, there is evidence that, at more severe grades of preterm birth, the difference between blacks and whites enlarges yet further (Figure 5). Whereas the relative risk of preterm delivery at 36–37 weeks among blacks compared to whites is 1.5, at 28 to 31 weeks, it is 3.1, and below 28 weeks, it is 3.8.

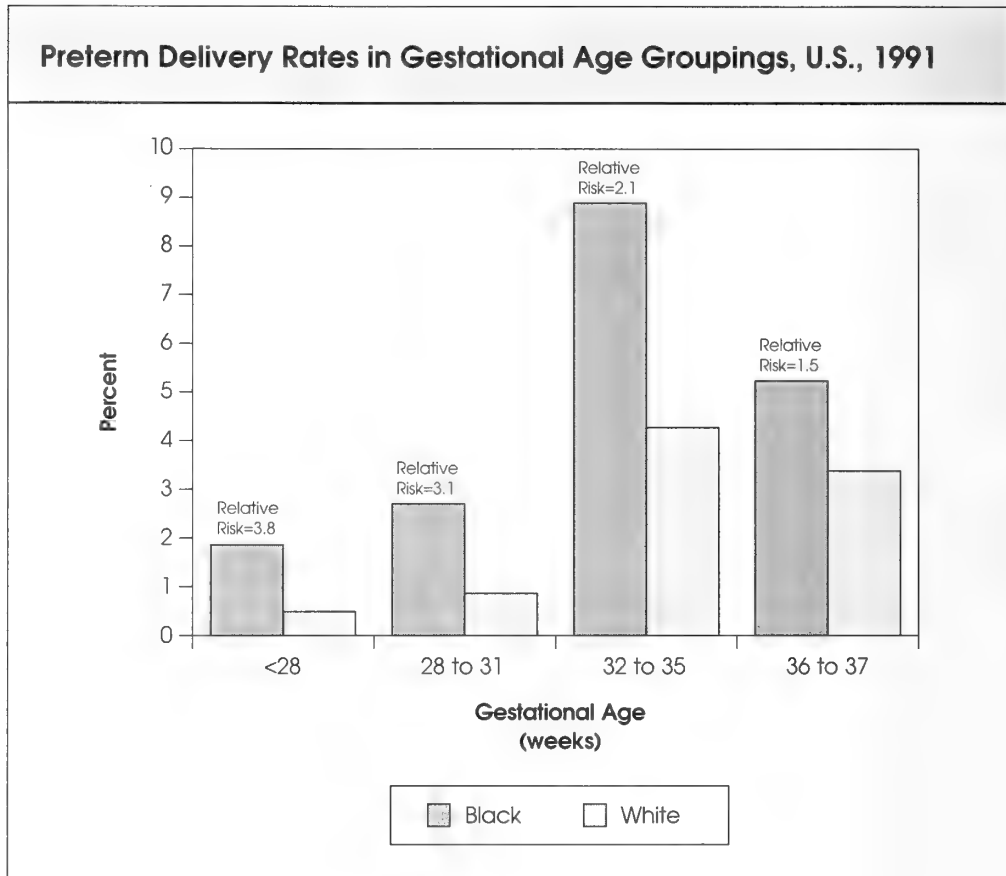
Of considerable interest is the observation that Mexican-American mothers in the United States have low birth weight and preterm births at virtually the same rate as the more privileged white population. The same is true for Native Ameri-

cans. The paradoxically different effects of social and economic deprivation in different ethnic groups is unexplained. A recent study indicates, however, that Mexican-American mothers living in poor, predominantly black neighborhoods in Chicago experience the high preterm birth rates characteristic of their African-American neighbors.³⁴ Thus, the protective qualities found among Mexican-American women are not immutable. Unraveling the underlying reasons for these ethnic variations in preterm delivery is one of the great challenges to public health research.

Secular Trends in Low Birth Weight, Preterm Delivery, and Infant Mortality

Figure 6 illustrates three secular trends in the United States over the past two decades—those in low birth weight (less than

Figure 5



Source: National Center for Health Statistics. *Advance report of final natality statistics, 1991*. Monthly Vital Statistics Report, Vol. 42, No. 3, Suppl. Hyattsville, MD: Public Health Service, 1993.

2,500 grams), preterm delivery (less than 37 weeks), and infant mortality. Broadly speaking, we can say that preterm delivery has not improved at all (and may be worsening very recently), low birth weight has improved slightly, and infant mortality has declined substantially. This recent disentanglement of infant mortality from its principal determinants is attributable to the operation of newborn intensive care and perhaps obstetric intensive care as well.³⁵ Simply put, babies now survive in much larger numbers than did babies of the same weight (and therefore the same intrinsic risk of death) in the past.

Preterm delivery, the principal cause of low birth weight in developed countries, appears to be on the rise in the United States. In 1991, 10.8% of U.S. births were preterm (born prior to 37 completed weeks of gestation), a rate 15% higher than the 1981 figure of 9.4%. It should be noted, however, that the increased use of more accurate techniques for dating the duration of pregnancy, particularly prenatal ultrasound, may have played some role in this reported rise. In addition, the Na-

tional Center for Health Statistics adopted, in 1981, a different method of allocating gestational age to birth certificates with uncertain gestational ages. This method is likely to have increased the proportion of infants classified as preterm.

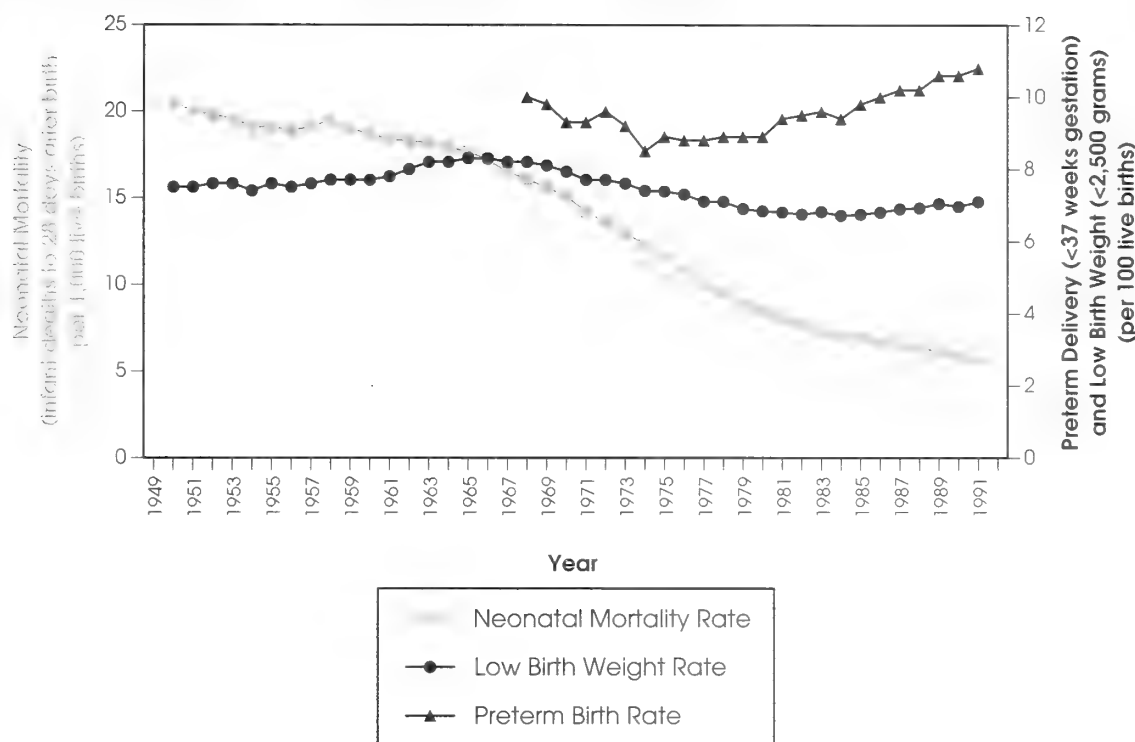
At least two conclusions of public policy significance can be drawn from the essential long-term stability in preterm delivery and low birth weight rates in the United States:

1. The recent epidemic of cocaine abuse cannot account for our high rates of these adverse reproductive outcomes. An excessive low birth weight rate was characteristic of the United States long before this particular drug epidemic. What most needs investigating are the socioeconomic dislocations that underlie drug-taking behavior.

2. Conventional prenatal care is not a solution to the problem of low birth weight in the United States. Currently, 85% of U.S. mothers present for prenatal care in the first trimester, a considerable improvement over past figures³⁶ and a proportion

Figure 6

Low Birth Weight, Preterm Birth, and Neonatal Mortality Rates in the United States, 1950–1991



Sources: Lee, K., Paneth, N., Gartner, L., et al. Neonatal mortality: An analysis of the recent improvement in the United States. *American Journal of Public Health* (1980) 80:15–21; National Center for Health Statistics. *Advance report of final mortality statistics*. Monthly Vital Statistics Report. Hyattsville, MD: Public Health Service. (1950 through 1991.); National Center for Health Statistics. *Advance report of final natality statistics*. Monthly Vital Statistics Report. Hyattsville, MD: Public Health Service. (1950 through 1991.)

which is higher than in Japan and Germany and only slightly lower than in Denmark and Norway.³⁷ Yet, low birth weight and preterm delivery stubbornly resist change.

Survival and Later Handicap

The striking improvement in survival at a given birth weight that has resulted from newborn intensive care has actually affected infants of all birth weights,³⁸ but the impact at the higher birth weights is less noticeable because mortality has always been quite low and survival, high. But at the very lowest birth weights, where survival was once the exception, the increase in rate of survival is so large that it is now having an impact on the childhood population.

For example, in the United States during 1960, 10,241 white singleton babies were born weighing less than 1,000 grams (2 pounds, 3 ounces), but only 67 of them

survived.³⁹ In 1983, 8,542 such infants were born, but 3,840 survived. In the space of 23 years, the number of survivors per 1,000 live births of this weight increased 70-fold. Each year many very low birth weight infants are now added to the population who would not previously have survived. Although the vast majority of these infants are healthy, enough of them have severe handicaps that their impact on the population prevalence of cerebral palsy is noticeable.⁴⁰

This raises an important question, one that assumes even greater significance as we contemplate the finances of health care reform. How much capital, both human and material, are we willing to invest to save the lives of the most extremely preterm infants? Even in babies as small as 500 to 600 grams, born at about 24 weeks of gestation, newborn intensive care can improve survival.⁴¹ But the costs of such interventions are extraordinary. These

costs include (for infants weighing 500 to 750 grams, or 1 pound, 2 ounces to 1 pound, 10 ounces) an average hospital stay of three to four months, much of which is spent on life-support equipment.⁴² Charges for the initial hospitalization for surviving infants weighing 500 to 600

course of action.⁴⁴ Others have advocated more strongly for instituting newborn intensive care whenever there is the possibility of improving survival.⁴⁵ The increasingly vocal concerns of family members ensure that these issues will be debated extensively outside as well as inside medical circles.⁴⁶

Charges for the initial hospitalization for surviving infants weighing 500 to 600 grams at birth averaged \$1 million in one study.

grams at birth averaged \$1 million in one study.⁴³ Moreover, although most of the 70% mortality in infants weighing 501 to 750 grams occurs early in life, with intensive care many of these such infants die only after as many as 100 days of hospitalization.⁴² The risk of severe handicap (cerebral palsy, mental retardation, epilepsy, blindness, or deafness) in survivors is about 20%, and of the nonhandicapped remainder, at least a third will experience substantial school difficulties.

There is no easy solution to the moral dilemmas posed by such difficult circumstances, but they must be confronted. One of the founders of neonatology, William Silverman, has eloquently argued that we must acknowledge the medical uncertainty of decisions about instituting intensive care in very preterm infants and permit parents more latitude to decide the

Conclusion

When the roots of a problem are clearly social and economic, it is tempting to rush in to provide a presumably preventive intervention before the essential scientific groundwork has been laid. But the provision of services, however well-intentioned, does not truly serve its recipients unless those services are effective. This places an obligation on those who would move quickly to public health action to show that the interventions work. Controlled trials have, by and large, failed to show effectiveness in preventing preterm birth, whether the intervention is social support,⁴⁷ enhanced prenatal care,⁴⁸ early recognition of labor,⁴⁹ or pharmacologic interruption of labor.⁵⁰ Honesty compels us to return to the drawing board of scientific investigation.

The problem of low birth weight is multifaceted; but from a public health perspective, the key goal is prevention of preterm birth. This goal cannot be achieved without a much better understanding than we currently have of the determinants of preterm delivery. The evolution of scien-

tific and clinical thought in this area has been slow, especially when compared with the rapid developments in treatment.

The essential work of distinguishing the components of low birth weight and preterm delivery, and their likely etiologic heterogeneity, has only just begun.^{51,52} While readily available social and demographic variables have been studied extensively for their relationship to low birth weight, a more in-depth pursuit of the nature of the relationship of poverty and social dislocation to low birth weight has not yet been undertaken. The effects of poverty at the level of the individual, the family, and the community need all to be taken account of; the context in which a pregnancy occurs is larger than the womb.

The special problem of preterm birth among African Americans needs focused attention, and such research will require innovative strategies.⁵³ It may be especially valuable to attempt to identify protective factors among African-American women otherwise at high risk.⁵⁴ At the same time, we must remember that no population is immune to preterm delivery and that clues to causation may also emerge from more detailed understanding of preterm delivery in the face of an apparently privileged environment. Even in Sweden, there is a social class gradient in preterm delivery.⁵⁵ Poverty must alter health through biological mechanisms, and much of the work of epidemiology consists of decoding the "biological expression of social stratification."⁵⁶

The mechanism or mechanisms of labor, both term and preterm, have not received as much scientific scrutiny as have many other biological processes of lesser public health significance. The role of sub-clinical infection in precipitating preterm labor, particularly when membrane rupture is the initiating event, clearly needs further exploration.^{57,58} Other interesting leads to pursue are the possible role of micronutrient deficiency,^{59,60} subtle pla-

The problem of low birth weight is multifaceted; but from a public health perspective, the key goal is prevention of preterm birth.

cental abnormalities signaled by elevated alpha fetoprotein levels,⁶¹ lead pollution,⁶² and conditions at work.⁶³ It is noteworthy that each of these mechanisms could plausibly explain part or all of the social class gradient in risk of preterm delivery.

In all of these endeavors, conflict between public health action and scientific research must be avoided as both unnecessary and counterproductive. In an eloquent essay, Paul Wise has recently underlined the need to reconcile the biologic and social etiologies of infant mortality. "The pursuits of efficacy and justice," Wise points out, "are inextricably linked."⁶⁴

1. Paneth, N. Recent trends in preterm delivery rates in the United States. *INSERM Colloque: Prevention of Preterm Birth* (1986) 138:15-30.
2. Ellenberg, J., and Nelson, K.B. Birthweight and gestational age in children with cerebral palsy or seizure disorders. *American Journal of Diseases of Children* (1979) 133:1044-48.
3. Bergman, I., Hirsch, R.P., Fria, T.J., et al. Causes of hearing loss in the high-risk premature infant. *Journal of Pediatrics* (1985) 106:95-101.
4. Gallo, J.E., and Lennerstrand, G. A population based study of ocular abnormalities in premature children aged 5 to 10 years: A regional study. *American Journal of Ophthalmology* (1991) 11:539-47.
5. Dunn, H.G., Robertson, A.M., and Crichton, J.V. Clinical outcome: Neurologic sequelae and their evolution. In *Sequelae of low birthweight: The Vancouver Study*. Clinics in Developmental Medicine series. H.G. Dunn, ed. London: Mac Keith, 1986, pp. 68-96.
6. Kraybill, E.N., Bose, C.L., and D'Ercole, A.J. Chronic lung disease in infants with VLBW. *American Journal of Diseases of Children* (1987) 141:784-88.
7. McCormick, M.C., Gortmaker, S.L., and Sobol, A.M. Very low birthweight children: Behavior problems and school difficulties in a national sample. *Journal of Pediatrics* (1990) 117:687-93.
8. Bergner, L., and Susser, M.W. Low birthweight and prenatal nutrition: An interpretive review. *Pediatrics* (1970) 46:946-66.

9. Stein, Z., Susser, M., and Rush, D. Prenatal nutrition and birth weight: Experiments and quasi-experiments in the past decade. *Journal of Reproductive Medicine* (1978) 21:287-99.
10. Rush, D., and Cassano, P. Relationship of cigarette smoking and social class to birth weight and perinatal mortality among all births in Britain, 5-11 April 1970. *Journal of Epidemiology and Community Health* (1983) 37:249-55.
11. Wegman, M.E. Annual summary of vital statistics—1992. *Pediatrics* (1993) 92,6:743-54.
12. Kleinman, J.C. The slowdown in the infant mortality decline. *Paediatric and Perinatal Epidemiology* (1990) 4:373-81.
13. Erickson, J.D., and Bjerkedal, T. Fetal and infant mortality in Norway and the United States. *Journal of the American Medical Association* (1982) 247:987-91.
14. Ericson, A., Eriksson, M., Westerholm, P., et al. Pregnancy outcome and social indicators in Sweden: The situation in a modern welfare state. *Acta Paediatrica Scandinavica* (1984) 73:69-74.
15. Klinger, A. Sociocultural factors associated with infant mortality and birthweight in Hungary. In *Proceedings of the international collaborative effort on perinatal and infant mortality*. Vol. III. DHHS/PHS 92-1252. Hyattsville, MD: National Center for Health Statistics, 1992, pp. IV-68-IV-77.
16. Rip, M.R., Sweeney, A.M., Paneth, N.S., et al. The epidemiology of preterm delivery among urban primiparous South African women, 1987-88. *Paediatric and Perinatal Epidemiology* (1993) 7:A20.
17. World Health Organization, Expert Committee on Maternal and Child Health. *Public health aspect of low birthweight*. WHO Technical Report Series, No. 27. Geneva, Switzerland: WHO, 1950.
18. National Center for Health Statistics. *Advance report of final natality statistics, 1991*. Monthly Vital Statistics Report, Vol. 42, No. 3, Suppl. Hyattsville, MD: Public Health Service, 1993.
19. Wang, X., Guyer, B., and Paige, D.M. Differences in gestational age-specific birthweight among Chinese, Japanese and White Americans. *International Journal of Epidemiology* (1994) 23:119-27.
20. Dawson, I., Golder, R.Y., and Jonas, E.G. Birthweight by gestational age and its effect on perinatal mortality in white and in Punjabi births. *British Journal of Obstetrics and Gynaecology* (1982) 89:896-99.
21. Ashford, J.R., Brimblecombe, F.S.W., and Fryer, J.G. Birthweight and perinatal mortality in England and Wales, 1956-65. In *Problems and progress in medical care*. G. McLachlan, ed. London: Oxford University Press, 1968, pp. 1-30.
22. Brimblecombe, F.S.W., Ashford, J.R., and Fryer, J.G. Significance of low birth weight in perinatal mortality: A study of variations within England and Wales. *British Journal of Preventive and Social Medicine* (1968) 22:27-55.
23. Wilcox, A.J., and Russell, I.T. Birthweight and perinatal mortality: I. On the frequency distribution of birthweight. *International Journal of Epidemiology* (1983) 12,3:314-18.
24. Wilcox, A.J., and Russell, I.T. Birthweight and perinatal mortality: II. On weight-specific mortality. *International Journal of Epidemiology* (1983) 12,3:319-25.
25. Wilcox, A.J., and Russell, I.T. Birthweight and perinatal mortality: III. Towards a new method of analysis. *International Journal of Epidemiology* (1986) 15,2:188-96.
26. Wilcox, A., and Russell, I.T. Why small black infants have a lower mortality than small white infants: The case for population-specific standards for birth weight. *Journal of Pediatrics* (1990) 116:7-10.
27. Kleinman, J.C. Implications of difference in birthweight distribution for comparison of birthweight-specific mortality. In *Proceedings of the international collaborative effort on perinatal and infant mortality*. Vol. III. DHHS/PHS 92-1252. Hyattsville, MD: National Center for Health Statistics, 1992, pp. V-28-V-43.
28. Chen, R., Wax, Y., Lusky, A., et al. A criterion for a standardized definition of low birthweight. *International Journal of Epidemiology* (1991) 20:180-86.
29. Kramer, M.S. Determinants of low birthweight: Methodological assessment and meta-analysis. *Bulletin of the World Health Organization* (1987) 65:663-737.
30. Parkin, J.M. The assessment of gestational age in Ugandan and British newborn babies. *Developmental Medicine and Child Neurology* (1971) 13:784-88.
31. Wilcox, A.J., and Skjoerven, R. Birth weight and perinatal mortality: The effect of gestational age. *American Journal of Public Health* (1992) 82:378-82.

32. Ounsted, M. Small-for-dates babies: A developmental update. *Paediatric and Perinatal Epidemiology* (1988) 2:203–7.
33. Hakim, R.B., Tielsch, J.T., and See, L.C. Agreement between maternal interview- and medical record-based gestational age. *American Journal of Epidemiology* (1992) 136:566–73.
34. Collins, J.W., and Shay, D.K. Prevalence of low birth weight among Hispanic infants with United States-born and foreign-born mothers: The effect of urban poverty. *American Journal of Epidemiology* (1994) 139:184–92.
35. Lee, K., Paneth, N., Gartner, L., et al. Neonatal mortality: An analysis of the recent improvement in the United States. *American Journal of Public Health* (1980) 80:15–21.
36. Racine, A.D., Joyce, T.J., and Grossman, M. Effectiveness of health care services for pregnant women and infants. *The Future of Children* (Winter 1992) 2:40–57.
37. Bergso, P., and Bakketeig, L.S. Overview of maternal and infant care in ICE countries and states. In *Proceedings of the international collaborative effort on perinatal and infant mortality*. Vol. III. DHHS/PHS 92–1252. Hyattsville, MD: National Center for Health Statistics, 1992, pp. III-3–III-16.
38. Buehler, J.W., Kleinman, J.C., Hogue, C.J.R., et al. Birthweight-specific infant mortality, United States, 1960 and 1980. *Public Health Reports* (1987) 102:151–61.
39. Paneth, N. Neonatal care and patterns of handicap in the community. *Clinics in Developmental Medicine* (1992) 123/124:232–41.
40. Bhushan, V., Paneth, N., and Kiely, J.L. Impact of improved survival of very low birthweight infants on recent secular trends in the prevalence of cerebral palsy. *Pediatrics* (1993) 91:1094–1100.
41. Allen, M.C., Donohoe, P.K., Dusman, A.E., et al. The limit of viability: Neonatal outcome of infants born at 22 to 25 weeks gestation. *New England Journal of Medicine* (1993) 329:1597–1601.
42. Hack, M., Horbar, J.D., Malloy, M.H., et al. Very low birth outcomes of the National Institutes of Child Health neonatal network. *Pediatrics* (1991) 87:587–97.
43. Pomerance, J.J., Pomerance, L.J., and Gottlieb, J.A. Cost of caring for infants weighing 500–749 g at birth. *Pediatric Research* (1993) 4:231A.
44. Silverman, W.A. Overtreatment of neonates? A personal retrospective. *Pediatrics* (1992) 90:971–76.
45. Robertson, N.R.C. Should we look after babies less than 800 g? *Archives of Disease in Childhood* (1993) 68:326–29.
46. Harrison, H. The principles for family-centered neonatal care. *Pediatrics* (1993) 92:643–50.
47. Elbourne, D., Oakley, A., and Chalmers, I. Social and psychological support during pregnancy. In *Effective care in pregnancy and childbirth*. I. Chalmers, M. Enkin, and M.J.N.C. Kierse, eds. Oxford: Oxford University Press 1989, pp. 221–36.
48. Alexander, G.R., Weiss, J., Hulsey, T.C., et al. Preterm birth prevention: An evaluation of programs in the United States. *Birth* (1991) 18:160–69.
49. Grimes, D.A., and Schultz, K.F. Randomized controlled trials of home uterine activity monitoring: A review and critique. *Obstetrics and Gynecology* (1992) 79:137–42.
50. Canadian Preterm Labor Investigators Group. Treatment of preterm labor with the beta-adrenergic agonist ritodrine. *New England Journal of Medicine* (1992) 327:308–12.
51. Ekwo, E.E., Gosselink, C.A., Wollson, R., et al. Risks for premature rupture of amniotic membranes. *International Journal of Epidemiology* (1993) 22:1–9.
52. Zhang, J., and Savitz, D.A. Preterm birth subtypes among Blacks and Whites. *Epidemiology* (1992) 3:428–33.
53. Rowley, D.L., Hogue, C.J.R., Blackmore, C.A., et al. Preterm delivery among African-American women: A research strategy. *American Journal of Preventive Medicine* (1993) 9(6 Suppl.):1–6.
54. Krieger, N., Rowley, D.L., Herman, A.A., et al. Racism, sexism and social class: Implications for studies of health, disease and well-being. *American Journal of Preventive Medicine* (1993) 9(6 Suppl.):82–122.
55. Bakketeig, L.S., Cnattingius, S., and Knudsen, L.B. Socioeconomic differences in fetal and infant mortality in Scandinavia. *Journal of Public Health Policy* (1993) 14:82–90.
56. This phrasing of a central goal of epidemiology is owed to David Rush, M.D. (personal communication).

57. Gibbs, R.S., Romero, R., Jillicr, S.L., et al. A review of premature birth and subclinical infection. *American Journal of Obstetrics and Gynecology* (1992) 166:1515–28.
58. Reynolds, H.D. Bacterial vaginosis and its implication in preterm labor and premature rupture of membranes. *Journal of Nurse-Midwifery* (1991) 36:289–96.
59. Scholl, T.O., Hediger, M.L., Fischer, R.L., et al. Anemia vs. iron deficiency: Increased risk of preterm delivery in a prospective study. *American Journal of Clinical Nutrition* (1992) 55:985–88.
60. Scholl, T.O., Hediger, M.L., Schall, J.I., et al. Low zinc intake in pregnancy: Its association with preterm and very preterm delivery. *American Journal of Epidemiology* (1993) 137:1115–24.
61. Weiner, C.P., Grant, S.S., and Williamson, R.A. Relation between second trimester alpha-fetoprotein and umbilical artery doppler velocimetry and their association with preterm delivery. *American Journal of Perinatology* (1991) 8:263–68.
62. McMichael, A.J., Vimpani, G.V., Robertson, E.F., et al. The Port Pirie cohort study: Maternal blood lead and pregnancy outcome. *Journal of Epidemiology and Community Health* (1986) 40:18–25.
63. Mamelie, N., Bertucat, I., and Munoz, F. Pregnant women at work: Rest periods to prevent preterm birth? *Paediatric and Perinatal Epidemiology* (1989) 3:19–28.
64. Wise, P. Confronting racial disparities in infant mortality: Reconciling science and politics. *American Journal of Preventive Medicine* (1993) 9(6 Suppl.):7–16.

The Direct Cost of Low Birth Weight

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Abstract

Medical and technological advances in the care of infants with low birth weight (less than 2,500 grams, or 5 pounds, 8 ounces) and very low birth weight (less than 1,500 grams, or 3 pounds, 5 ounces) have substantially increased the survival rate for these infants and have led to concerns about the demands their care places upon their families and society. The dollar cost of the resources used disproportionately to care for low birth weight children is one measure of the burden of low birth weight. Using analyses of national survey data for 1988 for children ages 0 to 15, this article presents estimates of the direct incremental costs of low birth weight—costs of the resources used to care for low birth weight infants above and beyond those used for infants of normal birth weight. In 1988, health care, education, and child care for the 3.5 to 4 million children ages 0 to 15 born low birth weight cost between \$5.5 and \$6 billion more than they would have if those children had been born normal birth weight. Low birth weight accounts for 10% of all health care costs for children, and the incremental direct costs of low birth weight are of similar magnitude to those of unintentional injuries among children and in 1988 were substantially greater than the direct costs of AIDS among Americans of all ages in that year.

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Almost all low birth weight infants (those born weighing less than 2,500 grams or 5 pounds, 8 ounces) require special attention. Although many function normally during childhood and beyond, they are more likely than children of normal birth weight to experience health and developmental problems. Recent medical and technological advances have increased the survival rate for the very tiniest infants and have led to increased concern about the demands these survivors place on their families and the rest of society (see the article by Tyson in this journal issue). Growth in the number of children born low birth weight, improvement in their rates of survival, and changes in medical technology and in the provision of medical and special nonmedical services to children with and at risk for various handicapping conditions have resulted in more services of various kinds for more surviving low birth weight children than ever before. There are costs associated with providing these services, however, and as the quantity of services increases, it is likely that these costs are also increasing.

With the growing prominence of cost concerns in health policy discussions, the costs of care for low birth weight and very low birth weight children are receiving increased attention.

Despite these concerns about costs, there have been few comprehensive attempts to document them. Fragmentation of the U.S. health care system presents a serious impediment to comprehensive cost assessment.¹ Funding has not been available to track representative samples of low birth weight children over time to assess long-term developmental and health outcomes. Costs of follow-up care and of assessments of outcomes are not fully covered by health insurance and, hence, are difficult to document. Moreover, low birth weight is not the qualifying condition for most of the medical and other services consumed disproportionately by low birth weight children, so it is impossible to identify and cost out the services they receive from most program budgets.

This article relies primarily on new analyses of data from several national surveys to estimate the incremental direct costs associated with low birth weight among children ages 0 to 15 in a single year, 1988. The focus is on incremental direct costs—costs that reflect resource utilization above and beyond the level of resources used by normal birth weight infants and children. Almost all of the costs

comprehensive national data on the costs of low birth weight in the areas of medical care, preschool programs, special education, and grade retention are all available. In 1988, there were between 3.5 and 4 million children ages 0 to 15 who had been born low birth weight. They accounted for almost 7% of children in that age group.²

Defining the Costs Associated with Low Birth Weight

The components of total cost for low birth weight include the costs of the medical care, special education, early intervention, and other support services consumed disproportionately by low birth weight children. Additional costs to the family, such as the extra time that parents of sick low birth weight babies devote to their care, are also components of the cost of low birth weight. In a cost-of-illness analysis, the different levels of resources associated with an illness or condition such as low birth weight are identified, quantified, and valued in money terms. Once they have been quantified and valued, the various components of cost can be summed to provide an estimate of the aggregate cost of the illness or condition and also the mean cost per case. When cost analyses are performed for a number of conditions, cost estimates for different conditions can be compared. (See Box 1 for definitions and descriptions of the cost-of-illness concepts applied in this article.)

Used properly, cost-of-illness research can aid decision making in several ways. First, it provides a means for combining many of the facets of a condition, such as the health and developmental problems experienced by some low birth weight children, into a single metric. This number is one measure of the size of the problem, and comparing the costs of a number of different problems may be particularly helpful in establishing priorities. Second, cost estimates can be helpful in evaluating proposed solutions. Because solutions have resource costs, knowing the cost of each solution may make it easier to decide which particular solution to pursue.

Growth in the number of children born low birth weight, improvement in their rates of survival, and changes in medical technology have resulted in more services of various kinds for more surviving low birth weight children than ever before.

analyzed are also incurred for children who are not low birth weight. Therefore, to determine incremental costs, those costs associated with being born normal birth weight are subtracted from the costs incurred by low birth weight children. From a policy perspective, such an analysis of aggregate incremental costs is particularly helpful in elucidating the gains that would occur from interventions which effectively reduce the frequency of low birth weight births. The focus is on 1988 because it is the most recent year for which

Previous Cost Studies

The most comprehensive economic evaluations of low birth weight are those published by a group of Canadian researchers in the early 1980s³ and by the Office of Technology Assessment (OTA) in 1988.^{4,5} In both of these studies, calculation of the costs associated with low birth weight was but one component in the evaluation of the cost-effectiveness of interventions designed to improve infant health. As part of an evaluation of neonatal intensive care, the Canadian researchers studied the mortality and morbidity of all very low birth weight infants (those weighing less than 1,500 grams, or 3 pounds, 5 ounces) born to residents of a southern Ontario county. The researchers estimated the cost of health care for these infants as well as the costs associated with their mortality and morbidity.⁶ The 1988 OTA evaluation focused on the savings that could accrue from the prevention of low birth weight births which might accompany expansion of the delivery of early prenatal care. The OTA did not attempt a comprehensive estimate of the cost of low birth weight.⁷ Instead, its report focused on the incremental costs of treating low birth weight babies in three categories: initial hospitalization including physician fees; rehospitalization in the first year of life (hospital costs only); and long-term costs of services (institutional care, foster care, early intervention, special education, and the like) provided for surviving low birth weight babies. Neither study reported estimates of the aggregate annual cost of low birth weight.

Incremental costs for very low birth weight births based on the Canadian study are reported in Table 1. Included are the mean cost per live birth of the initial hospitalization and calculated annual costs per survivor which incorporate birth-weight-specific infant mortality.⁸ Costs have been converted to U.S. dollars at the 1978 exchange rate and inflated to 1988 prices using the health care component of the gross domestic product (GDP) deflator.⁹ As can be seen in the table, the cost of the initial hospitalization (\$26,000) accounts for a substantial portion of the cost of very low birth weight identified in the Canadian study.

Table 1 also summarizes the midrange of the estimates of the incremental costs of a low birth weight birth based on data presented in the OTA report adjusted to 1988 dollars.⁹ Annual costs for ages 1 to

Box 1

Some of the Cost-of-Illness Concepts Used in this Article

Many studies have been done to determine the costs of illnesses. Such studies typically include calculations of direct health care costs, other costs not stemming from health care expenditures, and indirect costs due to foregone earnings. In estimating the costs of low birth weight, this article uses several different cost-of-illness concepts: tangible costs, direct costs, prevalence costs, and incremental costs. Understanding these concepts is important to the proper interpretation of the results.

Tangible costs: This article focuses only on tangible costs. These costs reflect a loss or diversion of resources that can be valued in the market and can be counted. Although many intangible costs result from the feelings and emotions of parents, children, and others touched by the sequelae of low birth weight, it is impossible to measure the depth of these feelings or to assign to them a dollar value.

Direct costs: These are the costs of goods and services consumed disproportionately by low birth weight children, such as the use of neonatal intensive care services. Because this article is limited to costs incurred during childhood, only direct costs are included. Not included are the indirect costs associated with the future loss of productivity that may be due to increased morbidity and mortality resulting from low birth weight.

Prevalence costs: This article focuses on prevalence costs, costs associated with all members of a specific and defined population in a particular year. Only costs incurred within that year are measured. Prevalence cost estimates are conceptually different from incidence cost estimates. An incidence cost estimate would include all lifetime costs of a cohort of low birth weight infants born in a single year. Although incidence costs are preferred for some policy purposes, they are inherently more difficult to perform and more prone to significant error because they require that projections of lifetime costs be made over many future years based on what is known at the present.

Incremental costs: Almost all of the costs analyzed are also incurred for children who are not low birth weight. The incremental costs reported here are costs above and beyond those incurred by normal birth weight infants and children. To determine incremental costs, the costs incurred by normal birth weight children are subtracted from estimates of total cost.

15 vary by age because of assumptions made by the OTA about the utilization of expensive services by children of different ages. In particular, for children 5 to 15 years, annual costs are increased by more than \$800 because of the inclusion of the costs of institutional and foster care for a small number of survivors. In addition, educational costs (including early intervention costs) are assumed to increase with advancing age.

The initial hospitalization costs reported in the OTA study are much less than those reported in the Canadian study

(\$6,200 versus \$26,000) in part because the OTA estimates are dominated by moderately low birth weight babies (those weighing 1,500 to 2,500 grams, or between 3 pounds, 5 ounces and 5 pounds, 8 ounces) who are much less expensive to care for than the very low birth weight babies (those weighing less than 1,500 grams), who were the subjects of the Canadian study. Following the same line of reasoning, it might be expected that the annual cost per survivor would have been much higher in the Canadian study than in the OTA report; however, the annual costs per survivor from the OTA and Canadian studies are roughly of the same order of magnitude (\$1,100 and \$1,500, respectively).

Both the Canadian and the OTA estimates have limited usefulness in assessing the aggregate cost of low birth weight in the United States today. The OTA esti-

reports on the health and developmental outcomes of low birth weight infants (see the article by Hack, Klein, and Taylor in this journal issue). They paint a detailed and varied picture of the experiences of low birth weight children. Many of these studies are of limited usefulness in assessing the aggregate cost of low birth weight because they are based on very limited samples that are not representative of the total population of low birth weight children and/or are of varying quality with regard to the nature of control and comparison groups, rates of attrition and duration of follow-up, and the measurement and classification of outcomes.

The classification of outcomes in many previous studies is particularly problematic for a cost study. Outcomes are typically identified in medical, neurological, and neuropsychiatric categories. These outcomes, such as abnormalities on neurological or physical examinations or reduced scores on tests of intelligence or psychomotor function, cannot be translated easily and directly into estimates of resource utilization which yield cost estimates. Even conditions such as cerebral palsy or blindness, both of which occur with greater frequency among low birth weight children, are complex and utilize resources in a number of different domains. In addition, more recently published follow-up studies of low birth weight infants look only at children with very low (less than 1,500 grams, or 3 pounds, 5 ounces), or extremely low (less than 1,000 grams, or 2 pounds, 3 ounces) birth weights. Such children represent less than 10% of all low birth weight births and an even lower percentage of surviving low birth weight children. Moreover, these children tend to have a higher frequency of problems than do children weighing 1,500 to 2,500 grams at birth. Hence, it is difficult to get a comprehensive picture of the costs of low birth weight from studies that focus solely on very low birth weight infants.

Since 1978, costs for very low birth weight babies have probably increased substantially in the aggregate and on a per-live-birth and per-survivor basis.

mates exclude additional medical care costs for noninstitutionalized children age one and older, are quite sensitive to assumptions about the degree of institutional and foster care received by low birth weight children, and exclude all costs of "mild" impairments. The Canadian estimates reflect the Canadian health and education systems, which differ significantly from the systems found in the United States. In addition, both studies reflect health and developmental outcomes from the mid- to late 1970s and, therefore, do not account for the impact of new technologies introduced since then. For example, since 1978, infant survival rates for extremely low birth weight infants (those weighing less than 1,000 grams, or 2 pounds, 3 ounces) have more than doubled, and survival has also improved considerably for babies weighing 1,000 to 1,499 grams.¹⁰ As a result, costs for very low birth weight babies have probably increased substantially in the aggregate and on a per-live-birth and per-survivor basis.

In addition to the Canadian and OTA studies, there are a multitude of published

Costs of Low Birth Weight

Data Sources and Methods

To obtain a fairly complete and balanced estimate of the medical care costs of low birth weight babies during the first year of life, data from two recently published estimates of the costs of health care for infants^{11,12} and claims data from the CIGNA Corporation's national employer-based business survey are combined.¹³ Because

Table 1

Incremental Direct Costs of Very Low Birth Weight and Low Birth Weight Children from Birth to Age 15 in 1988 Dollars from Two Studies		
	Cost per Live Birth, 1988 Dollars	Annual Cost per Survivor, 1988 Dollars
Costs for very low birth weight children (<1,500 grams) based on 1973–1976 Canadian experience		
Cost of initial hospitalization	\$26,000	
Mean annual costs from initial discharge to age 15		\$1,500
Health care costs		1,000
Other costs		450
Costs for all low birth weight babies (< 2,500 grams) based on 1988 OTA report		
Cost of initial hospitalization	6,200	
Rehospitalization costs in first year (hospital only)		910
Annual costs ages 1 to 15, including institutionalization, foster care, early intervention, special education		
Ages 1 to 3		260
Age 4		490
Ages 5 to 10		1,400
Ages 11 to 15		1,400
Mean annual cost ages 1 to 15		1,100

Sources: Calculations by the authors from data presented in Boyle, M., Torrance, G., Sinclair, J., and Horwood, S. Economic evaluation of neonatal intensive care of very-low-birth-weight infants. *New England Journal of Medicine* (June 2, 1983) 308:1330–37; U.S. Congress, Office of Technology Assessment. *Healthy children: Investing in the future*. OTA-A-345. Washington, DC: U.S. Government Printing Office, February 1988.

the CIGNA data are derived from a privately insured population, they cannot be used directly to provide an unbiased estimate of the incremental costs of care of low birth weight infants.¹⁴ To control for possible sources of bias, the CIGNA data were first used to estimate the relative first-year costs of health care for babies in three groups (normal birth weight, extremely premature, and all other low birth weight). Next, these birth-weight-specific cost ratios were weighted by the actual distribution of births by weight in the 1988 U.S. birth cohort. Then, these population-weighted relative cost ratios were applied to an estimate of aggregate national expenditures on health care for infants in 1988 to allocate expenditures between low birth weight and normal birth weight infants.¹⁵

The remainder of this analysis relies primarily on previously published and unpublished analyses of incremental resource use derived from two nationally representative population surveys, the 1988 Child Health Supplement of the National Health Interview Survey (CHS-NHIS) and the 1991 National Household Education Survey's (NHES) Pre-primary and Primary Surveys.¹⁶ Information about a child's birth weight is available in both surveys, and the relatively large number of children included allows for analyses of age-appropriate resource utilization (preschool programs for children ages 3 to 5, special educational programs for those ages 6 to 15, grade repetition for those ages 11 to 15, and hospitalization for children of all ages). Using estimated levels of

resource utilization by birth weight category, it was possible to assign costs to the resources used. All of the estimates presented are from multivariate statistical analyses which control for the effects of possible confounding variables, such as income or mother's education, which might otherwise bias measurement of the net effect of low birth weight.¹⁷

These surveys are not without their limitations. First, they are based on parental report and therefore are subject to errors of recall, interpretation, and reporting. Second, information about all facets of resource use by children is not available or has not been analyzed. Last, although the surveys contain a large number of observations of low birth weight children, there are few observations of very low and extremely low birth weight children. Because the likelihood of experiencing a significant, chronic condition increases substantially as birth weight declines, the costs of low birth weight may be underestimated if an analysis relies exclusively on studies using national population surveys.^{18,19}

Estimates of health care costs used in this article are also based largely on a previously published analysis of expenditures from the 1987 National Medical Expenditure Survey (NMES), a national survey of roughly 35,000 individuals in 4,000 households in the United States.¹¹ To provide an estimate of the aggregate cost of low birth weight, estimates of the various sources of incremental cost per low birth weight child were multiplied by estimates of the number of low birth weight children in age groups 3 to 5, 6 to 11, and 11 to 15. Estimates of the number of low birth weight children in each age group came from the 1988 CHS-NHIS.²⁰

Medical Costs in the First Year of Life

According to our assessment, of the estimated \$11.4 billion spent on health care for infants in 1988, 35%, or \$4.0 billion, was for the incremental costs incurred by low birth weight infants (Table 2). On a per-infant basis, this amounted to almost \$15,000 additional for each of the 271,000 infants born weighing less than 2,500 grams in 1988. A general trend of higher costs in lower birth weight babies is documented in the table. Total costs for extremely premature infants (those weighing less than 1,000 grams or experiencing respiratory distress syndrome) were almost three times as great as costs for other low birth weight babies (\$33,900 versus \$11,900). These babies accounted for more than 45% of the incremental costs associated with low birth weight. Babies with birth weights between 1,000 and 2,500 grams without respiratory distress syndrome were, on average, six times as costly as normal birth weight babies (\$11,900 versus \$1,900). Incremental costs associated with the care of these babies accounted for 19% of the annual cost of health care for infants in the United States.

The figures presented in Table 2 are reasonable estimates of the costs of health care for infants and of the incremental costs associated with low birth weight births. However, there is considerable variation in cost estimates for both of these statistics reported in a variety of sources.²¹ These differences may result, in part, from using data from different years in an area of health care where technology has been changing rapidly. Although data from different years are, for purposes of comparison, typically adjusted with a price index, using a price index to adjust cost estimates from different years may not be adequate if changes in costs are being driven primar-

Table 2

Health Care Costs During the First Year of Life by Birth Weight Among All U.S. Infants in 1988^a				
Birth Weight Group	Number of Births, 1988	Incremental Cost per Birth, 1988 Dollars	Total Incremental Cost, 1988 Dollars (billions)	Percentage of Total Health Care Costs for Infants
Normal birth weight (≥2,500 grams)	3,600,000	\$ 1,900	\$ 7.40 ^b	65%
Low birth weight (<2,500 grams)	271,000	15,000	4.00	35%
Extremely low birth weight ^c	57,000	32,000	1.80	16%
Other low birth weight ^d	214,000	10,000	2.20	19%

^a Columns and rows may not add or multiply exactly because individual entries have been rounded.

^b Includes nonincremental costs of 271,000 low birth weight babies.

^c Includes infants weighing 1,000 grams or less at birth or being diagnosed as having respiratory distress syndrome.

^d Includes infants weighing 1,000 to 2,500 grams without respiratory distress syndrome.

Sources: Calculations by authors from data presented in Lewit, E.M., and Monheit, A.C. Expenditures on health care for children and pregnant women. *The Future of Children* (Winter 1992) 2:2:95-114; Long, S.H., Marquis, M.S., and Harrison, G.R. The cost and financing of perinatal care in the United States. *American Journal of Public Health* (September 1994) 84:9:1473-78; Cholet, D.J., Newman, Jr., J.F., and Sumner, A.T. The corporate cost of poor birth outcomes. In *Infant health in America: Everybody's business*. Hartford, CT: CIGNA, 1992. pp. 3-23.

ily by changes in technology.²² Differences may also result from comparing estimates of costs with those of charges, from using data from different parts of the country when there are substantial regional variations in costs, and from comparing estimates that are more or less inclusive of physician, outpatient, and rehospitalization costs.

Costs During the Preschool Years

The preschool period can be a critical time for many low birth weight infants. For those who survive infancy with chronic health problems, utilization of health care services will remain high and access to appropriate specialized services will be important, although not always realized. A number of studies of low birth weight children demonstrate that they often perform poorly on psychological and developmental assessments compared with their normal birth weight peers, but little is known about how this reduced performance translates into resource utilization to support them during the preschool years.²³

Most studies of low birth weight preschool children have focused on limited,

defined cohorts of children in special programs or treated neonatally at particular institutions. Few studies have examined how these children fare in the general population.²⁴ Accordingly, analyses of recent general population data, the 1988 CHS-NHIS, and the 1991 NHES were undertaken as background to this article to understand more fully the resources utilized by low birth weight and other medically at-risk children during their preschool years.²⁵

These analyses are summarized in this article with emphasis on what they indicate about the resource utilization of children ages three to five. All the analyses discussed below used multivariate statistical techniques to control for the effects of variables other than low birth weight on health status and the utilization of special services.

Health Care Utilization

Analysis of the 1988 CHS-NHIS demonstrated that low birth weight significantly increased the probability of hospitalization among three- to five-year-olds. Low birth weight children ages three to five are

Table 3

Incremental Direct Costs of Low Birth Weight Among Children from Birth to Age 15 in 1988				
Age Group	Cost Type	Mean Cost per Low Birth Weight Child in Each Age Group ^a 1988 Dollars	Number of Low Birth Weight Children in Each Age Group ^b	Total Costs, 1988 Dollars
Infancy	Health care	\$15,000	271,000 ^c	\$4,000,000,000
1 to 2 years	All	N/E ^d	500,000	N/E ^d
3 to 5 years	Health care	290	820,000	240,000,000
3 to 5 years	Child care	180	820,000	150,000,000
6 to 10 years	Health care	470	1,300,000	610,000,000
6 to 15 years	Special education	150	2,400,000	360,000,000
11 to 15 years	Grade repetition	45	1,100,000	50,000,000
Total			4,000,000	\$5,400,000,000

Sources:

^a Cost per low birth weight child: Calculations by authors from data presented in this article.^b Number of low birth weight children (<2,500 grams): Unpublished data from the 1988 Child Health Supplement to the National Health Interview Survey.^c The number of low birth weight children under age one comes from birth certificate data for 1988 from the Vital Statistics System and is consistent with the figure in Table 2 in this article. The Child Health Supplement to the National Health Interview Survey counts 223,814 infants in this group for 1988. (See note no. 2 in the endnote section of this article.)^d N/E=not estimated. Costs for this age group are not presented in this article.

not only almost twice as likely to be hospitalized as normal birth weight children but also spend more time in the hospital once admitted. The combination of these effects results in low birth weight children ages three to five spending almost four times as much time per year in the hospital as their normal birth weight peers.²⁵ Annual mean expenditures on both physicians and hospitals for inpatient care of all children ages 3 to 12 were approximately \$112 (1988) based on the 1987 NMES.¹¹ Increased rates of hospital utilization by low birth weight children ages three to five result in an incremental cost per child of \$290 and an aggregate incremental cost of approximately \$240 million²⁶ (see Table 3).

Other Resource Effects

Analyses of both the 1988 CHS-NHIS and 1991 NHES showed that having a low birth weight child had no effect on whether a mother works or the child attends some kind of child care, on the type of child care (family or center-based), on secondary child care arrangements, or on changes in child care arrangements during the pre-

vious year.²⁵ Two findings, however, did have resource implications. First, there was evidence that low birth weight children are more likely to delay entry into kindergarten. Because low birth weight children are as likely to attend preschool as their normal birth weight peers, this result indicates that low birth weight children consume more preschool resources than their normal birth weight peers. However, the net effect of this difference appears quite small.

Although low birth weight children ages three to five appear no more likely to be enrolled in preschool programs than normal birth weight children, there is some evidence that low birth weight children may receive more or higher quality, and thus more costly, preschool instruction. Results from the 1991 NHES indicated that low birth weight children who attend preschool programs tend to be in programs with higher adult-child ratios, about 18% above the ratios reported for normal birth weight children.²⁵ Because about 35% of children attend preschool

or nursery programs, this increased staffing ratio may have important cost implications. If the costs of these programs are roughly proportional to the adult-child staffing ratio, costs for low birth weight children enrolled in these programs may be 18% higher than costs for normal birth weight children. Based on an average cost of \$2,900 per child in preschool programs, the incremental cost per low birth weight child in preschool would be \$520.²⁷ If 35% of the approximately 820,000 low birth weight children ages three to five are enrolled in these programs, the total cost would be \$150 million per year in 1988 dollars (see Table 3).

The finding that low birth weight had no measurable effect on whether a child's mother worked warrants additional discussion because it contradicts the results of several previous studies, which found that mothers of children with chronic health conditions are less likely to work.²⁸ There are at least two possible reasons for this difference. First, although low birth weight children may have a higher frequency of health problems than normal birth weight children, their health problems on average are less severe than the conditions of children with specific, identified, major chronic conditions who were the subjects of these previous studies. Second, most publicly funded handicapped preschool programs, which provide an opportunity for mothers to work, were not initiated until after the earlier studies were conducted. The latter factor is a potentially important caveat attendant to most of the preceding discussion of programs for preschool children. Publicly funded preschool programs for children with handicaps or other special needs have been undergoing substantial expansion in recent years and are scheduled to continue to grow. Determining whether these programs serve low birth weight children disproportionately will require further study.²⁹

Costs Among School-Aged Children

This section examines the incremental costs associated with the health, school performance, and behavioral outcomes of low birth weight children when they are in school. The focus is on the 6- to 15-year-old age group. Those under 6 are addressed in the discussion of preschoolers, and those 16 and older are excluded because school performance and the decision to drop out of school are probably related.

This complicates the analysis of the effect of low birth weight on those 16 and over.³⁰

A number of studies have examined the functioning of low birth weight children into their school years. Most of these studies have found that low birth weight children have average health and function normally in school.³¹ There is evidence, however, of a higher incidence of neurologic impairments or chronic health conditions in the low birth weight group, and they also exhibit a greater likelihood of experiencing difficulties in school. Most studies, however, do not estimate the costs associated with these problems among low birth weight children, and many are based on samples of children in one geographic location.³²

For this article, empirical analyses of the effects of low birth weight among school-aged children, based on data from the 1988 CHS-NHIS, were used to make cost estimates.^{30,33} This data set allows for multiple measures of outcomes and makes it possible to control for the effects of confounding variables.³⁴ Costs associated with reduced health status, special education, and grade retention among 6- to 15-year-olds who weighed less than 2,500 grams at birth were estimated.

Health Care Costs

Corman and Chaikind used the 1988 CHS-NHIS to examine the effect of low birth weight on a number of measures of health status and health care utilization among school-aged children.³⁰ They performed separate analyses for children ages 6 to 10 and those ages 11 to 15. They found that, in general, low birth weight children do not necessarily outgrow many of their health problems as they mature. Parents of these children are more likely to report that they experienced a number of health problems from a nine-item checklist and that they are limited in some range of activities. The analysis also shows that children who were low birth weight are more likely to be absent from school, but the magnitude of this effect, less than one day per year on average, is not large.

One particularly costly health effect associated with low birth weight is an increased use of inpatient hospital care among children ages 6 to 10. On average, it appears that low birth weight children in this age group spend about 0.5 more nights in the hospital per year for illness than normal birth weight children. This difference is substantial in relative terms:

the mean number of nights in the hospital per annum for all 6- to 10-year-olds in the CHS-NHIS is 0.12.³⁰ Corman and Chaikind do not report on other measures of health care utilization in their analyses, but it appears not unreasonable to expect that low birth weight children use other health services more than normal birth weight children given the increased level of health problems they experience. The magnitude of this potential increased level of health care utilization is difficult to estimate and may be small on average.³⁵

In estimating the incremental health care costs of low birth weight among school-aged children, a conservative approach is taken and only the costs directly associated with increased hospitalization among 6- to 10-year-olds are counted. Data from the 1987 NMES suggest that annual per capita expenditures on care in the hospital for children 3 to 12 years old were \$112 in 1988 dollars including hospital and physician charges.¹¹ Thus, the incremental cost per low birth weight child ages 6 to 10 was about \$470 in 1988. For the approximately 1.3 million low birth weight children in this age group, the total cost was \$610 million per year in 1988 dollars (see Table 3).

Schooling Costs

The performance of low birth weight children in school is important for several reasons. First, school is the primary activity of children, and schools have the opportunity to help compensate for deficiencies

Children ages 6 to 15 who weighed less than 2,500 grams at birth were almost 50% more likely than normal birth weight children to be enrolled in some type of special education program.

associated with low birth weight that may linger. Second, school performance is an important predictor of how children will function as adults. Also, substantial resources are expended on children's education, and disproportionate utilization of special services by low birth weight children may have significant economic implications.

School performance may be measured by standardized intelligence and/or achievement tests, grades, parent ratings, teacher ratings, grade repetition, and identification as a special needs student.

Studies show differences between low birth weight and normal birth weight children on many of these measures, but the differences with the most obvious cost implications are in the areas of special education and grade retention. These areas are the focus of the balance of this section.

■ *Special Education*

Several studies have identified the increased use of special education services among low birth weight children relative to normal birth weight children. One, using data from the 1988 CHS-NHIS, found that, after controlling for a number of individual, family, and regional factors, children ages 6 to 15 who weighed less than 2,500 grams at birth were almost 50% more likely than normal birth weight children to be enrolled in some type of special education program.³³ The analysis also indicated that low birth weight children appeared to be 64% more likely to be enrolled in special education classes than normal birth weight children if only medical factors are controlled for.³⁶

The increased utilization of special education by low birth weight children can have a significant impact on the cost of these programs and on the cost of education generally. Data released in the late 1980s showed that the average national total per pupil expenditure on special education was \$6,335 in the 1985–86 school year and that the excess cost of special education for all programs, defined as the total per-pupil cost for special education less the total per-pupil cost for regular education, was \$3,555 per pupil in the same year.³³ Estimates of the annual incremental special education costs associated with low birth weight range from \$447 million to \$244 million in 1988–1989 dollars; however, only the best estimate of \$360 million is reported in Table 3.³⁷ This estimate includes the costs associated with all types of special education and controls for a number of family and socioeconomic factors which can affect placement in special education.

■ *Grade Repetition*

Low birth weight children are not only more likely to use special education services than normal birth weight children, they are also more likely to repeat a grade in school. Another study, also based on the 1988 CHS-NHIS, found that, particularly for children ages 11 to 15, low birth weight children, whether in special education or not, are more likely to have repeated a

grade at some point in their schooling than normal birth weight children.³⁰

In general, the likelihood of grade repetition tends to increase for all children regardless of birth weight the longer they attend school. Therefore, one way to measure the effect of low birth weight on grade repetition is to ask how many more low birth weight children will repeat a grade by the time secondary schooling is completed than those who were not low birth weight. About 31% of low birth weight children will repeat a grade by grade 10 compared with about 26% of normal birth weight children.³⁰

There are costs associated with this higher rate of grade repetition among low birth weight children. The average per pupil cost of repeating a grade has been estimated at more than \$4,000.³⁸ If 5% of the approximately 250,000 low birth weight survivors born every year repeat at least one grade strictly because of low birth weight, the resulting cost may exceed \$50 million per cohort.³⁹ This incremental cost is incurred each year as members of successive cohorts of low birth weight children move through the nation's education system and experience slightly elevated annual rates of grade repetition that cumulate in a five percentage point differential relative to normal birth weight children by grade 10.

Grade retention may also be an important marker for future costly life experiences. Evidence suggests that students who are retained for a grade are substantially more likely to drop out of school than children who are not retained. In general, high school dropouts tend to have lower earnings, commit more crimes, and require more social services than high school graduates and those who go on to college.³⁸ However, no attempt is made in this article to attribute any of the costs attendant to these postschool experiences to low birth weight.

Discussion

The incremental costs associated with low birth weight exceeded \$5.4 billion in 1988 (see Table 3). Of these costs, almost 75% (\$4.0 billion) were due to the health care cost of infants. The balance was associated with increased health care, specialized child care, and education costs among children 3 to 15 years of age.

The costs of low birth weight may be underestimated in this article. With the exception of the medical costs in the first year of life, estimates are based on rates of utilization of resources inferred from national surveys. Accordingly, costs that have not been identified in these surveys were not taken into account. For example, costs for one-year-olds (see Table 3) were not

About 31 % of low birth weight children will repeat a grade by grade 10 compared with about 26 % of normal birth weight children.

included. However, there is reason to believe that incremental costs are associated with low birth weight in this age group. Data from the Infant Health and Development Program (IHDP), a major controlled trial to evaluate the effects of early intervention programs on low birth weight children ages zero to three years, indicate that one- and two-year-olds in both the experimental and control groups of that trial averaged about 0.15 hospitalizations per year.⁴⁰ This rate of hospitalization is more than twice as high as rates of hospitalization reported for all one- to four-year-olds in the National Hospital Discharge Survey.⁴¹ This finding of increased rates of hospitalization among low birth weight one- and two-year-olds is also consistent with findings, reported in this article, of increased rates of hospital use among low birth weight infants and 3- to 11-year-olds. Because this article is limited to cost estimates derived from nationally representative data sources, an estimate of the incremental costs (\$50 to \$60 million per year based on the IHDP data) associated with increased hospitalizations among low birth weight one- and two-year-olds is not included in the estimate of incremental costs. Estimates of increased health care costs, other than those associated with hospitalization for low birth weight children age one and older, also are not included, although there is reason to believe that considerable ambulatory care costs are associated with low birth weight in this age group.⁴²

Errors may also result from failure to account adequately for the costs associated with infrequent but very costly conditions associated with low birth weight, the costs borne directly and indirectly by the families of low birth weight children but

not identified in national surveys, and the costs of services, such as early intervention programs, which were just being phased in at the time of the surveys used in this analysis.

Important costs resulting from severely debilitating conditions associated with low birth weight not specifically addressed in this article are the costs of long-term care in hospitals, schools, and other institutions for the chronically ill, mentally re-

The costs of developmental services are not inconsequential and may be an important source of incremental expenditures on handicapped low birth weight children.

tarded, and physically handicapped (institutionalization) and the costs of developmental services. Differential rates of institutionalization for low birth weight children cannot be measured in the CHS-NHIS, NHES, or NMES data sets used in this analysis. Costs of institutionalization were, however, an important component of the OTA's estimate of the costs of low birth weight, accounting for almost half of the costs for 5- to 15-year-olds reported in Table 1.⁴ The OTA's estimate, however, was not based on hard data about rates of institutionalization of low birth weight children. Instead, it reflected a range of assumptions about the likelihood that severely impaired children would be institutionalized. Based on data from a more recent report, which used data from California to estimate the costs of 11 major birth defects, it was determined that the cost of institutionalization accounted for about 16% of the annual incremental cost of cerebral palsy.⁴³ Cerebral palsy, although much more prevalent among low birth weight children than among those born weighing more than 2,500 grams, is relatively rare (about 1.7 cases per 100 children).⁴⁴ Moreover, rates of institutionalization among 0- to 15-year-olds for all health-related reasons are very low in the United States today. Accordingly, it is unlikely that the estimates presented here are seriously biased by failure to account for institutionalization among low birth weight children.⁴⁵

Developmental services, which include day care programs, case management and counseling, and respite care for clients

and their families, supplement traditional medical care for seriously handicapped individuals and may, in some cases, substitute for institutionalization. The costs of developmental services are not inconsequential and may be an important source of incremental expenditures on handicapped low birth weight children which we have not measured adequately in this study. The costs of developmental services have been estimated to account for 9% to 14% of the total incremental costs of cerebral palsy exclusive of the costs of institutionalization.⁴³ Low birth weight children with cerebral palsy are more likely to receive developmental services than the majority of low birth weight children who typically experience conditions that are less severe or not disabling. However, given that other high-cost conditions associated with low birth weight may require developmental services similar to those provided for children with cerebral palsy, the cost estimates reported in Table 3 may understate the costs of low birth weight by 5% to 10%.

Other potentially undercounted costs are those borne directly by families due to modification of everyday activities to accommodate the disproportionate care needs of low birth weight children. These costs originate in the added expense of travel to the hospital to visit low birth weight infants who remain in care after their mothers are discharged and include other costs associated with increased utilization of health care services by some low birth weight children after their initial hospitalization.⁴⁶ An important part of the travel costs is the time foregone by parents from other activities. Parents' time foregone from other activities is also an important component of the cost of the additional care many low birth weight babies require. Some of these costs have been documented for small samples of families with very low birth weight infants and for families of chronically ill and severely disabled children,⁴⁷ but the burden associated with these costs for low birth weight children as a group has yet to be determined. Incremental expenditures on nonhealth goods and services such as transportation, clothing, diet, laundry, and baby-sitting may be of considerable importance for some families of low birth weight children with significant handicaps, but these costs also have not been well documented.²⁸ On the other hand, some family costs such as out-of-pocket

expenditures for health care, a significant burden for some families, are probably included in the health care cost estimates. Other costs, such as reduced labor force participation of mothers of disabled children, may be less important today than previously as publicly financed child care in handicapped preschool and enrichment programs releases family members from child care duties to pursue market activities.⁴⁸

Important new activities that may involve low birth weight children disproportionately but may be underrepresented in the surveys relied on for this analysis are the new early intervention programs mandated by the 1986 amendments to the Education of the Handicapped Act (now known as the Individuals with Disabilities Education Act, or IDEA). Part H of the act provides federal assistance to states for early intervention services for very young children (birth to age 3) with handicaps and their families.⁴⁹ The federal grants support coordination of services across agencies to ensure that comprehensive early intervention services are available on a statewide basis. States are allowed flexibility in defining developmental delay and may include those children at risk of delay.⁵⁰ Given the increased risk of disability for low birth weight children, they are more likely to be eligible for Part H programs than are normal birth weight children. Most of the costs of Part H programs probably have not been captured in this article because the data used are from time periods before the full implementation of the new programs in most states and before any implementation in other states and because the surveys used in these analyses did not ask questions about participation in special preschool programs except Head Start.⁵¹

Just as some developments may increase the measurable cost of low birth weight, other developments may reduce these costs. Evidence is accumulating that the rapid and widespread adoption of exogenous surfactant to treat low birth weight babies may not only increase survival but may also save medical care costs during the very expensive first few months of life. A recent study of the effect of surfactant on resource use in newborn infants weighing 500 to 1,500 grams found that the introduction of surfactant in the late 1980s reduced inflation-adjusted charges for babies who survived by approximately 10%.⁵² Charges also declined for babies

who died, but the reduction, although large, was not statistically significant. Extrapolating these changes to the national level and adjusting for the costs associated with an increase in the survival rate yields an estimate of the cost savings attributable to surfactant of \$2,760 per very low birth weight infant.⁵³

It may well be that babies treated with surfactant will have better health outcomes generally so that costs after discharge from the NICU will also be reduced. Similarly, it may be that cost savings will be realized in the future if the early intervention programs implemented under Part H prove to be as effective in widespread implementation as some have been demonstrated to be in particular situations.⁵⁴

All things considered, it appears likely that the cost of low birth weight (\$5.4 billion in 1988—see Table 3) may be underestimated by at least 10% primarily because of failure to account for very costly special services (long-term care and developmental services) used disproportionately by severely handicapped low birth weight children and early intervention and other special services for very young children. This suggests that the cost of low birth weight may have exceeded \$6.0 billion in 1988. Recognition of the high costs associated with a relatively small number of severely handicapped children also underscores the fact that estimates of mean expenditures per low birth weight child may be misleading. Costs for low birth weight children with specific handicapping conditions may be at least an order of magnitude higher than the average costs reported in Table 3.⁵⁵ On a population basis, these high-cost children are balanced by the large number of low birth weight children without significant, costly pathology. For the families of severely incapacitated children, however, these costs are real and speak to the need for either private insurance and/or public programs to provide financing not only for acute medical care but also for the costly and diverse array of services these children require.

Comparison with Other Health Problems

The incremental cost of low birth weight—\$5.4 (and perhaps more than \$6.0) billion in 1988—while a substantial number, is more meaningful when compared with estimates of the direct costs of other important health problems. As can be seen in the

top panel of Table 4, the annual direct cost of low birth weight is about one-third the annual direct cost of smoking and two-thirds the direct cost of alcohol abuse. The deleterious consequences of smoking and alcohol abuse fall primarily on older and middle-aged Americans, however, while low birth weight primarily impacts families with young children. Unintentional injuries are the leading cause of death in children after infancy (see the Child Indicators article

The annual direct cost of low birth weight continues to exceed the cost of AIDS.

in this journal issue) and appear to be about as costly as low birth weight. In contrast, the annual direct cost of low birth weight was several times the annual direct cost of AIDS among persons of all ages in 1988 and, although the cost of AIDS has grown very rapidly since 1988, the authors believe that the annual direct cost of low birth weight continues to exceed the cost of AIDS.⁵⁶ AIDS has received much public attention and increased research funding in recent years.

The bottom panel of Table 4 presents another illustration of how cost-of-illness estimates can be used to facilitate decision making, examination of the incremental contribution of low birth weight to national costs. As can be seen in the table, the incremental health care costs of low birth weight account for approximately 10% of annual health care expenditures on children. Interventions which effectively reduce the rate of low birth weight would release these resources either to attack other health problems or for non-health uses. About 75% of the costs of low birth weight are incurred in the care of infants, so interventions that reduce the number of low birth weight births can have an immediate and important effect on costs. Costs incurred by older children will, however, be reduced more gradually as the birth cohorts with reduced rates of low birth weight age. Reducing the rate of low birth weight births will have a smaller relative impact on the nation's education budget than on the health budget. The incremental costs of low birth weight ac-

count for only 2% of the special education budget and only 0.2% of the total expenditures on education. Moreover, most of the savings in education costs will not be realized for many years after a reduction in the number of low birth weight births. Potential savings in special programs for children ages zero to five years of age which result from a reduction in the number of low birth weight births may be realized more rapidly than savings in school-aged children, but quantifying the extent of these potential savings is problematic at this point in time.

Ultimately, the real costs of low birth weight are the costs experienced by human beings who are not able to realize their potential. The costs that have been counted and attributed to low birth weight in this article primarily measure the value of the resources society currently expends in an effort to compensate for low birth weight among children. But, despite the resources expended on compensatory activities during infancy, childhood, and youth, many low birth weight children reach adulthood with a disproportionate share of health and developmental problems. Although the extent and severity of these problems have yet to be accurately measured, the evidence suggests that residual problems experienced by adults who were born at low birth weight may be large in terms of increased morbidity, lost earnings, and increased demand for health and social services.⁵⁷

From a public policy perspective, the cost estimates presented in this report suggest that the aggregate annual costs of low birth weight are of a similar order of magnitude as other health problems which have received public attention in recent years. Moreover, the payback from programs that are effective at reducing the prevalence of low birth weight should be quite rapid. The key action step is to identify such interventions and then provide the resources and leadership to see that they are effectively implemented.

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Table 4

Cost of Low Birth Weight in Perspective		
Comparison of Annual Direct Cost of Low Birth Weight to Annual Direct Costs of Other Major Health Problems		
Health Problem	Age	Cost, 1988 Dollars (millions)
Smoking	all ^a	\$ 17,000
Alcohol abuse	all ^a	9,100
Low birth weight	0 to 15	5,400–6,000*
Injuries	0 to 14 ^b	5,500
AIDS	all ^c	1,800–2,400**
Contribution of Low Birth Weight to National Costs of Services for Children		
Service	Cost, 1988 Dollars (millions)	Percentage of Total Cost Due to Low Birth Weight
Health care for children ^d	\$ 53,000	
Low birth weight health care	4,900–5,400*	9–10%
Special education ^e	17,000	
Low birth weight special education	360	2%
Total education ^f	209,000	
Low birth weight grade retention and special education costs	410	2%
*Range of estimates reflects potential underestimate of costs for very high-cost children.		
**Range of estimates reflects variation in published estimates of costs of AIDS.		

Sources:

- ^a Horgan, C., Marsden, M.E., and Larson, M.J. Substance abuse: The Nation's number one health problem: Key indicators for policy. Princeton, NJ: Robert Wood Johnson Foundation, 1993, p. 16, Chart 4.
- ^b Rice, D.P., and Mackenzie, E.J. Cost of injury in the United States: A report to Congress. San Francisco: Institute for Health and Aging, University of California, and Baltimore, MD: Injury Prevention Center, Johns Hopkins University, 1989, p. 89, Table 20.
- ^c See note no. 56 at the end of this article for a more complete description of estimates of the cost of AIDS.
- ^d Lewit, E.M., and Monheit, A. Expenditures on health care for children and pregnant women. *The Future of Children* (Winter 1992) 2.2:95–114.
- ^e Chaikind, S., Danielson, L.C., and Brauen, M.L. What do we know about the costs of special education? A selected review. *Journal of Special Education* (1993) 26.4:344–70, p. 361, Table 5.
- ^f National Center for Education Statistics, Department of Education. Telephone conversation with Vance Grant, November 20, 1994.

1. Data on charges for care in neonatal intensive care units (NICUs) may be available, but the costs of physician care in the NICU and during subsequent hospital stay after discharge from the unit are typically billed separately and may not be available. Moreover, a high proportion of sick low birth weight babies are transferred between hospitals (sometimes several times), and it is difficult to track the costs associated with care in different institutions because universal identifiers to facilitate the tracking of these transferred infants typically do not exist. This same factor makes identification and attribution by birth weight of the costs of rehospitalization of infants problematic. As a result of the complexities of hospital accounting systems, third-party payment arrangements, and cross-subsidized care, hospital charge data, particularly for small samples of infants or for a single institution, may not provide good estimates of the actual cost of the care provided.

2. Data from the 1988 Child Health Supplement to the National Health Interview Survey, which are used throughout this analysis, suggest there were nearly 4 million (3,955,496) surviving children ages 0 to 15 who were born low birth weight. To test the validity of these data, the number of low birth weight children in each age group was calculated using data from the Vital Statistics System and other sources, subtracting the number of deaths from births for each birth weight category for the years 1973 to 1988. (National Center for Health Statistics. *Advance report of final natality statistics, 1987*. Monthly Vital Statistics Report, Vol. 38, No. 3, Suppl. Hyattsville, MD: Public Health Service, 1989, p. 24, Table 11; National Center for Health Statistics. *Health, United States, 1992*. Hyattsville, MD: Public Health Service, 1993, pp. 21, 22, 36, Tables 7, 8, 19; National Center for Health Statistics. *Health, United States, 1987*. Washington, DC: Public Health Service, 1988, p. 36, Table 7; Unpublished tables from the Vital Statistics System; National Center for Health Statistics, Mortality Division. Telephone conversation with Ken Kochanek, December 7, 1994; Unpublished data from New York State.) This exercise resulted in a total of 3,535,650 surviving low birth weight children ages 0 to 15 in 1988. While the figures do not match exactly, they are close enough to give confidence that the number of low birth weight children ages 0 and 15 was between 3.5 and 4 million in 1988.
3. Boyle, M., Torrance, G., Sinclair, J., and Horwood, S. Economic evaluation of neonatal intensive care of very-low-birth-weight infants. *New England Journal of Medicine* (June 2, 1983) 308:1330–37.
4. U.S. Congress, Office of Technology Assessment. *Healthy children: Investing in the future*. OTA-A-345. Washington, DC: U.S. Government Printing Office, February 1988, pp. 212–35.
5. The Institute of Medicine included an analysis of some of the effects of low birth weight on health care expenditures in its 1985 report *Preventing low birth weight*. Washington, DC: National Academy Press, 1985.
6. For neonatal care, the actual costs at the three hospitals providing neonatal care in the Ontario county studied were reported. These were supplemented with information on physician charges and other neonatal health care costs, and the costs of resources consumed by children after their initial discharge from the hospital including both health care and other costs (institutional care, special services, special education, and the like). Parents were interviewed to determine the types, sources, and costs of services used by surviving children. Because longer-term outcomes were not observed for the younger children at the time of the study, costs were forecast for children in the intensive care groups. Also reported in the original publication are projected lifetime earnings and health care costs to death, typically as an adult.
7. The OTA used many secondary data sources to construct its estimates. Hospital costs from the state of Maryland for newborn care by birth weight category were used to estimate initial hospitalization costs. Physician charges for NICU care, however, were estimated as a percentage of hospital charges, and rehospitalization costs were based on a study of rehospitalization rates of a sample of low birth weight babies and the national average daily cost for a hospital stay. (McCormick, M.C., Bernbaum, J.C., Eisenberg, J.M., et al. Costs incurred by parents of very low birth weight infants after the initial neonatal hospitalization. *Pediatrics* [September 1991] 88,3:533–41.) Long-term health care costs were even more difficult to estimate. Cost estimates were based on population estimates of the prevalence of moderate and severe disabilities among low birth weight babies at age one and of the cost of services provided, by level of disability, to severely and moderately mentally retarded people (most of whom were not low birth weight).
8. Estimated annual costs per survivor are calculated by dividing undiscounted costs from discharge to age 15 by estimated life-years per live birth. Life-years per live birth (11.1 years for infants weighing 1,000 to 1,500 grams and 3.4 years for infants weighing 500 to 999 grams) is a measure of survival to age 15. This calculation assumes that costs after discharge are spread evenly over the first 15 years of life.
9. The Gross Domestic Product (GDP) deflator is a commonly used statistical index that can be used to adjust for the effects of inflation. It is used here to adjust dollar values for years other than 1988 to be comparable to those for 1988. See U.S. Department of Commerce. *Statistical Abstract of the United States, 1993*. 113th ed. Lanham, MD: Bernan, 1993.
10. Birth-weight-specific infant survival rates for New York State, exclusive of New York City, were 29 per 100 for babies weighing less than 1,001 grams, 81 per 100 for babies weighing between 1,001 and 1,500 grams, and 88 per 100 for babies weighing from 1,501 to 2,500 grams in 1980. By 1990, birth-weight-specific survival rates for these same groups had increased to 52 per 100, 93 per 100, and 95 per 100, respectively. (New York State Department of Health. Personal correspondence with Timothy Smith, August 11, 1994.)

11. Lewit, E.M., and Monheit, A.C. Expenditures on health care for children and pregnant women. *The Future of Children* (Winter 1992) 2,2:95–114.
12. Long, S.H., Marquis, M.S., and Harrison, G.R. The cost and financing of perinatal care in the United States. *American Journal of Public Health* (September 1994) 84,9:1473–78.
13. The claims data represent all maternity-related and infant claims for a 24-month period between September 1, 1989, and August 31, 1991. Information about the charges incurred by almost 59,000 mother-infant pairs is included in the data. Six diagnosis-related group (DRG) categories reported on the claims record were used to describe the birth status of the infants. Three DRGs identified low birth weight and/or premature infants. Claims for up to one year of postdelivery care of infants in the various DRG categories are used to estimate the relative cost of care for infants of different birth weights during the first year of life. Chollet, D.J., Newman, Jr., J.F., and Sumner, A.T. The corporate cost of poor birth outcomes. In *Infant health in America: Everybody's business*. Hartford, CT: CIGNA, 1992, pp. 3–23.
14. Private insurance companies, such as CIGNA, have traditionally reimbursed health care providers (doctors, hospitals, and others) for charges that tend to exceed costs, in part to cross-subsidize discounted and uncompensated care. Hence, national estimates based on extrapolations of insurance claims data may substantially overstate the cost of care for infants. In addition, privately insured births may not be a representative sample of all births in the United States. The socioeconomic, racial, geographic, and physiological makeup of a sample of insured births is likely to underrepresent high-risk babies as compared with the national birth cohort.
15. Specifically, the CIGNA data were used to obtain estimates of the relative cost of care for infants in three groups: all normal birth weight babies, extremely premature babies (those weighing less than 1,000 grams (2 pounds, 3 ounces) at birth or diagnosed with respiratory distress syndrome, and all other low birth weight babies. In 1988, some 3.6 million babies were born weighing more than 2,500 grams, 23,762 weighing less than 1,000 grams, and 246,919 weighing 1,000 to 2,499 grams. There are no national data on the number with respiratory distress syndrome (RDS). This number was estimated as follows: Data from the Vermont-Oxford Neonatal Network suggest that about 80% of extremely low birth weight babies suffer from RDS. Data from the CDC (Becerra, J.E., Fry, Y.W., and Rowley, D.L. Morbidity estimates of conditions originating in the perinatal period: United States, 1986 through 1987. *Pediatrics* [September 1991] 88,3:553–59) suggest that 19.2% of all low birth weight babies have RDS. Applying these percentages to the 1988 birth data provided an estimate of the number of babies weighing 1,000 to 2,499 grams who had RDS (32,961). Adding this estimate to the number of extremely low birth weight babies and subtracting it from the number of babies weighing 1,000 to 2,499 grams yielded estimates of the number of babies born in 1988 in each of the three groups—normal, extremely premature, and other low birth weight. These population estimates were next multiplied by the relative cost weights derived from the CIGNA claims data. The resulting product was then divided into the estimate of the cost of infant care, \$11.4 billion, in 1988. (Lewit and Monheit [see note no. 11] estimated expenditures on health care for infants in 1987 at \$12.6 billion. Long, Marquis, and Harrison [see note no. 12] estimated the cost of infant care at \$10.1 billion in 1989. The mean of these two estimates, \$11.4 billion, was used to derive an estimate of the cost of health care for low birth weight infants.) The resulting quotient was an estimate of the cost of care of a normal birth weight baby (reported in Table 2). This estimate was then multiplied by the relative cost weights derived from the CIGNA data for extremely premature and other low birth weight babies to obtain estimates for the mean costs of care for infants in these groups. These estimates, less the estimated first-year cost of a normal birth weight baby, are reported as the incremental cost estimates in Table 2.
16. The Child Health Supplement of the 1988 National Health Interview Survey (CHS-NHIS) is a large nationally representative survey which contains detailed information on the health, school performance, and behavior of children as well as information on their birth weight and demographic and socioeconomic characteristics. It includes extensive information about health, medical conditions, health care utilization, child care arrangements, and maternal employment. The results of studies based on the 1988 CHS-NHIS of the use of health care and special education services and grade repetition by children of different birth weights are used in this analysis. The 1991 National Household Education Survey's (NHES) Pre-primary and Primary Surveys, which collected information on 6,700 children ages three to five who range from no schooling to grade 2, are used to examine the effect of birth weight on the use of preschool programs and maternal labor force participation. The surveys contain less information on health status than the CHS-NHIS but far more detailed information on preschool child care arrangements, including Head Start programs.
17. Other variables controlled in these analyses include race/ethnicity, region of residence, residence in a rural or urban area, age, and gender.

18. An earlier analysis of low birth weight children using the 1981 CHS-NHIS addressed a similar concern arising from the small number of very low birth weight children in that data set. Examination of the excess morbidity due to low birth weight showed, however, that most of this morbidity was attributable to children with moderately low birth weight (from 1,500 to 2,499 grams, or from 3 pounds, 5 ounces to 5 pounds, 8 ounces) and not the tiniest infants. (Overpeck, M.D., Hendershot, G.E., Hoffman, H.J., and Moss, A.J. A comparison of the childhood health status of normal birth weight and low birth weight infants. *Public Health Reports* (January/February 1989) 104,1:58–70.)
19. In addition, information about birth weight is not available for those over 17 years of age, and information about those ages 16 and 17 may be somewhat unreliable because the number of low birth weight respondents is small. Therefore, findings for children older than 15 years are not reported.
20. A potential problem with the CHS-NHIS estimates is that they might underestimate the number of low birth weight children because the sampling frame does not include children in long-term care facilities and other institutions. However, the CHS-NHIS estimates are consistent with population estimates based on national vital statistics.
21. For an example of the variability of these estimates, compare them with the OTA and Canadian estimates in Table 1. Also, data from New York State suggest that, in 1991, the mean hospital charge for the initial hospitalization of low birth weight infants in that state was \$12,000 (1988 dollars) compared with a charge of \$1,100 for normal birth weight babies (tabular data provided by William Kelly, Center for Health Policy Studies, July 26, 1994). Data from a 1985 stratified sample of urban hospitals showed that low birth weight infants represented 9% of the neonatal patient load but consumed 57% of the aggregate cost of neonatal hospital care. Neonates weighing 500 to 1,499 grams accounted for more than one-third of costs in the same sample. In 1988 dollars, the mean cost for a normal birth weight neonate in the sample was \$850; for a low birth weight neonate, costs averaged \$9,600; and for extremely low birth weight babies, costs averaged \$34,000. Schwartz, R. What price prematurity? *Family Planning Perspectives* (July/August 1989) 21,4:170–74. Unpublished data from California for 1984–1987 suggest mean costs for the initial hospitalization of very low birth weight singleton live births in the Medicaid population were more than \$55,000 in 1988 dollars. This estimate includes the cost of stays at more than one hospital for babies who were transferred during their initial hospitalization. (RAND Corporation. Telephone conversation with and fax from Jeanette Rogowski, July 13, 1994.)
22. Lewit and Monheit (note no. 11) report that a substantial portion of the increase in the cost of care for infants between 1977 and 1987 cannot be explained by price changes or population growth. It appears to have resulted from technological change that increased survival among low birth weight infants. As discussed in the text, the total cost of care for surviving high-risk infants is typically much higher than the cost of care for similar infants who die.
23. Crowe, T.K., Deitz, J.C., Bennett, F.C., and TeKolste, K. Preschool motor skills of children born prematurely and not diagnosed as having cerebral palsy. *Journal of Developmental and Behavioral Pediatrics* (August 1988) 9,4:189–93; Mazer, B., Piper, M.C., and Ramsay, M. Developmental outcome in very low birth weight infants 6 to 36 months old. *Journal of Developmental and Behavioral Pediatrics* (October 1988) 9,5:293–97; Rose, S.A., Feldman, J.F., Rose, S.L., et al. Behavior problems at 3 and 6 years: Prevalence and continuity in full-terms and preterms. *Development and Psychopathology* (1992) 4,3:361–74; Szatmari, P., Saigal, S., Rosenbaum, P., et al. Psychiatric disorders at five years among children with birth weights less than 1000g: A regional perspective. *Developmental Medicine and Child Neurology* (November 1990) 32,11:954–62.
24. An exception is the analysis of the 1981 CHS-NHIS performed by statisticians at the National Institutes of Health (see note no. 18). At the time of their analysis, the 1981 CHS-NHIS was the most comprehensive data base of a representative sample of U.S. children reflecting aspects of their lives as related to their health status. Health status was represented in the 1981 study by lifetime chronic conditions, hospital stays, bed days, and limitations on activity. The analysis of children under age six found that not all the reported differences between low birth weight and normal birth weight children were statistically significant. However, a pattern of increased frequencies of persistent health problems among low birth weight children was documented on a number of different measures. For those indicators that have implications for resource utilization (bed days and hospital stays), the differences are statistically significant and large. The rates for low birth weight children are approximately twice the rates for those of normal birth weight. For example, 10.5% of low birth weight children had two or more hospital stays, compared with 4.8% of normal birth weight children. Although these findings from the 1981 CHS-NHIS are quite suggestive, much has changed since these data were collected. Survival rates for low birth weight infants have risen

steadily, hospitalization rates for children have declined steadily, and the scope and availability of child care programs of a general and specialized nature have mushroomed. For these reasons, the 1981 data should be interpreted with caution in discussions of the costs of low birth weight today.

25. Corman, H. The effects of low birth weight and other medical risk factors on resource utilization in the preschool years. Report to the Center for the Future of Children, June 1994.
26. Corman's research using the 1988 CHS-NHIS (see note no. 25) suggests that low birth weight children ages three to five average 0.23 days in the hospital per year compared with a mean of 0.06 days for normal birth weight children of the same age. Data from the 1987 NMES suggest expenditures of \$112 (1988) per child ages 3 to 12 for both physician and hospital charges associated with inpatient care (see note no. 11, Lewit and Monheit). Assuming that the cost of the incremental increase in hospitalization for low birth weight children is proportional to the cost of hospitalization for all three- to five-year-olds results in an incremental cost of \$290 per low birth weight child in this age group and an aggregate cost of \$240 million based on approximately 820,000 low birth weight children in the United States in this age group in 1988 (see note no. 2).
27. The estimated cost of \$2,900 comes from the 1990 National Child Care Survey and represents the average yearly price that families with working mothers pay for all types of child care programs (\$3,260) deflated to 1988 dollars (Galinsky, E., and Friedman, D.F. *Education before school: Investing in quality child care*. New York: Scholastic, 1993, p. 86). Because it includes payments for all types of child care programs, and not just part-day preschool or nursery school programs, it may be an overestimate of the costs. Unfortunately, information on the costs of part-day programs is not readily available. However, there is reason to believe that this estimate is fairly close. Partly because of differences in staff salaries, the costs of part-day programs tend to be very similar to those of full-day programs (National Association for the Education of Young Children. Telephone conversation with Barbara Willer, November 21, 1994). In addition, Head Start, which is a program included in these cost estimates, had an average federal payment of \$2,700 per child in 1988, quite near the \$2,900 survey estimate (Administration on Children, Youth, and Families. *Project Head Start: Statistical fact sheet*. Washington, DC: U.S. Department of Health and Human Services, January 1993, p. 3).
28. A number of these studies are summarized in Salkever, D.S. Parental opportunity costs and other economic costs of children's disabling conditions. In *Issues in the care of children with chronic illness*. N. Hobbs and J.M. Perrin, eds. San Francisco: Jossey-Bass, 1985. Salkever notes that the finding of reduced labor market participation by mothers of children with chronic health conditions has not been uniformly reported for all family types, income levels, and racial groups. While the reasons income or race may influence the effects of children's handicaps on parental labor supply is unclear, it appears that small sample sizes in certain population subgroups make reliable measurement of any effect difficult. In addition to the negative effect children's ill health has on maternal labor force participation, it appears that mothers of chronically ill children also earn less per hour worked.
29. Moreover, the availability and growth of these programs has been uneven in different parts of the country. Thus, surveys conducted in the late 1980s and early 1990s may have underestimated the need for these services and the eventual enrollment in these programs once they become fully disseminated and operational. Data being collected today and in the future may similarly underestimate the need for and costs of these special preschool programs until they are expanded to meet adequately the demand for their services.
30. Corman, H., and Chaikind, S. *The effect of low birth weight on the health, behavior and school performance of school-aged children*. Working Paper No. 4409. Cambridge, MA: National Bureau of Economic Research, July 1993.
31. See, for example, Smith, A.E., and Knight-Jones, E.B. The abilities of very low birth weight children and their classroom controls. *Developmental Medicine and Child Neurology* (July 1990) 32,7:590-601; Drillien, C.M., Thomson, A.J., and Burgoyne, K. Low birth weight children at early school age: A longitudinal study. *Developmental Medicine and Child Neurology* (February 1980) 22,1:26-47.
32. Geographically restricted samples may result in several sources of error in assessing the impact of low birth weight. First, estimates of the actual prevalence of health, learning, and behavioral problems may be biased if the sample of children is not adequately representative of the national population of children. Second, the availability of health and education programs and resources may vary geographically with the result that measures of program participation in one area may not be generalizable to other areas.
33. Chaikind, S., and Corman, H. The impact of low birth weight on special education costs. *Journal of Health Economics* (1991) 10:291-311.

34. Such statistical control is extremely important to obtaining unbiased estimates of the incremental effect of low birth weight. Low birth weight births tend to occur more frequently among lower socioeconomic population groups. Children from these groups may have health and school problems largely unrelated to birth weight. Failure to control for these confounders could lead to an overestimate of the cost of low birth weight. In fact, the impact of socioeconomic factors on the well-being of children is so strong that some researchers have concluded that, by the time children reach a certain age, the consequences of socioeconomic factors completely overwhelm birth weight in determining well-being (see the article by Hack, Klein, and Taylor in this journal issue). However, the studies reviewed in this article suggest otherwise.
35. For example, an analysis of the effects of low birth weight in the 1981 CHS-NHIS found increased rates of hospital utilization among low birth weight children but no differences in the frequency of doctor visits between low birth weight children and those of normal birth weight (see note no. 18, Overpeck, Hendershot, Hoffman, and Moss).
36. Hence, the analysis gives some support to the notion that the school-related problems low birth weight children encounter with greater frequency than normal birth weight children are, in part, attributable to socioeconomic factors associated with increased low birth weight. However, the evidence also suggests that the differential utilization of special education by low birth weight children cannot be attributed primarily to social factors.
37. Chaikind and Corman (see note no. 33) report cost estimates for the 1989–90 school year. The figures reported in the text are their estimates adjusted to 1988–89 dollars using the GDP deflator.
38. Shepard, L.A., and Smith, M.L. Synthesis of research on grade retention. *Educational Leadership* (May 1990) :84–88.
39. In 1988, approximately 250,000 low birth weight infants survived, according to birth and death data from the Vital Statistics System. Because of increasing success in saving low birth weight babies, the total number of survivors has increased over time. For example, in 1973 there were about 210,000 infant survivors, and in 1983 there were about 231,000 infant survivors (see note no. 2 for data sources).
40. McCormick, M.C., Brooks-Gunn, J., Shapiro, S., et al. Health care use among young children in day care: Results in a randomized trial of early intervention. *Journal of the American Medical Association* (May 1, 1991) 265,17:2212–17.
41. Information from the National Center for Health Statistics, Data Dissemination Branch. November 22, 1994.
42. Shankaran, S., Cohen, S.N., Linver, M., and Zonia, S. Medical care costs of high-risk infants after neonatal intensive care: A controlled study. *Pediatrics* (1988) 81,3:372–78.
43. Waitzman, N.J., Scheffler, R.M., and Romano, P.S. *Cost of birth defects*. Lanham, MD: University Press of America. (In press.) Waitzman, N.J., Scheffler, R.M., and Romano, P.S. Estimates of the economic cost of birth defects. *Inquiry* (Summer 1994) 31:188–205.
44. The incremental prevalence, or the prevalence above and beyond the prevalence for normal birth weight children, of cerebral palsy among low birth weight children is 1.6 per 100. Bhushan, V., Paneth, N., and Kiely, J.L. Impact of improved survival of very low birth weight infants on recent secular trends in the prevalence of cerebral palsy. *Pediatrics* (June 1993) 91,6:1094–1100.
45. According to unpublished data from the U.S. Bureau of the Census, approximately 54,000 children ages 0 to 15 were institutionalized in 1990. More than 50% of these placements appear to be in “juvenile institutions” such as reform schools. If low birth weight children were four times as likely as normal birth weight children to be institutionalized in health care facilities, the cost of their institutionalization would be approximately \$160 million per year at a cost of \$50,000 per institutionalized child.
46. McCormick, M.C., Stemmler, M.M., Bernbaum, J.C., and Farran, A.C. The very low birth weight transport goes home: Impact on the family. *Journal of Developmental and Behavioral Pediatrics* (1986) 4:217–23; McLoughlin, A., Hillier, V.F., and Robinson, M.J. Parental cost of neonatal visiting. *Archives of Disease in Childhood* (1993) 68:597–99.
47. Leonard, B., Brust, J.D., and Sapienza, J.J. Financial and time costs to parents of severely disabled children. *Public Health Reports* (May/June 1992) 107,3:302–12. See also, note no. 28, Salkever, and note no. 46, McCormick, Stemmler, Bernbaum, and Farran.
48. From the cost measurement perspective, if new services substitute for services previously provided by the family, additional costs are not incurred. The source and burden of the costs make it easier to measure these costs, and as a result, they may begin to appear in cost analyses.

49. Office of Special Education and Rehabilitative Services. Meeting the needs of infants, toddlers, and preschool children with disabilities. In *Implementation of the Individuals with Disabilities Education Act: Fifteenth annual report to Congress*. Washington, DC: U.S. Department of Education, 1993, pp. 45–86.
50. Bowden, J.D., Black, T., and Daulton, D. *Estimating the costs of providing early intervention and preschool special education services*. Springfield, VA: EDRS, 1990.
51. As reported in September 1993, 18 states had fully implemented Part H beginning in 1991, 23 were planning implementation beginning in Fiscal Year 1992, and 12 states requested a second year of extended participation for planning because they were not yet able to meet the federal requirements for full implementation of the program. (Office of Special Education Programs. Telephone conversation with Jim Hamilton, October 20, 1994.) Some low birth weight children were, however, undoubtedly being served in many states under state programs in the late 1980s. Even if the time period of these surveys overlapped with the phase-in of Part H, low birth weight is very unlikely to have been a single criterion for admission to the new programs. Being labeled “handicapped” by one’s family has been found to be correlated with more special education services of all kinds, but not all low birth weight children are handicapped, and many have disabilities that parents may not consider to be a “handicap.” Programs aimed at early intervention which use at-risk children as their eligible population are likely to have higher proportions of low birth weight children involved, but the costs of that involvement are unknown. Future efforts to measure the participation of low birth weight children in Part H programs and other new or expanded programs targeted to at-risk children may lead to increases in the measured but not the actual costs of low birth weight, even if the actual cost of low birth weight represented by participation in similar but previously uncounted programs does not change appreciably.
52. Schwartz, R.M., Luby, A.M., Scanlon, J.W., and Kellogg, R.J. Effect of surfactant on morbidity, mortality, and resource use in newborn infants weighing 500 to 1,500 g. *New England Journal of Medicine* (May 26, 1994) 330,21:1476–80.
53. According to Schwartz, Luby, Scanlon, and Kellogg (see note no. 52), the mean total charges per very low birth weight infant (survivors and those who died) was \$50,700 before the widespread use of surfactant. The mean charge dropped to \$45,900 in the postsurfactant period. This charge reduction of \$4,800 per infant corresponds to a cost savings of \$2,800 per infant after applying the cost-to-charge ratio of 0.57 reported in the article.
54. Infant Health and Development Program Staff. Enhancing the outcomes of low birth weight, premature infants: A multisite randomized trial. *Journal of the American Medical Association* (1990) 58:3035–42.
55. For example, estimated annual costs for 3- to 14-year-olds with cerebral palsy are approximately \$13,000 (see note no. 43, Waitzman, Scheffler, and Romano), more than ten times the average costs presented in Table 3, page 42 in this journal issue, for all low birth weight children.
56. Published estimates of the cost of AIDS, although lower than our estimate of the cost of low birth weight in 1988, are highly variable. Changing methods and levels of treatment, rapidly increasing rates of disease, and changes in the definition of AIDS make it difficult to compare the costs of AIDS to the cost of low birth weight. Much of the difficulty is related to sheer numbers. Between 1988 and 1992, the number of low birth weight births increased about 6%, while the number of living people with AIDS increased over 150%. Therefore, the static measure presented here for 1988 cannot be interpreted as a projection into the future. The authors estimate that, after adjustment for inflation and the growth in the prevalence of low birth weight and AIDS, the direct incremental cost of low birth weight was approximately \$7.4 billion in 1992 and the direct cost of AIDS about \$3.4 billion in the same year. It is conceivable that the direct cost of AIDS may eventually approach more closely or even exceed the cost of low birth weight in the future.

The estimate for the cost of AIDS sums the nonpersonal direct costs of AIDS with the product of the cost per case and the number of cases using data from two studies of the costs of AIDS and data on the number of cases reported from the Centers for Disease Control and Prevention. (See Hellinger F.J. Updated forecasts of the costs of medical care for persons with AIDS, 1989–93. *Public Health Reports* (Jan.–Feb. 1990) 105,1:1–12; Scitovsky A.A., Rice D.P. Estimates of the direct and indirect costs of Acquired Immunodeficiency Syndrome, 1985, 1986, and 1991. *Public Health Reports* (Jan.–Feb. 1987) 102,1:5–17; and per telephone conversation with information specialists at the HIV/AIDS Technical Information Office, Centers for Disease Control, February 22, 1995. The authors’ estimate of the number of cases of AIDS in 1988 is the mean of the cumulative number of people alive and diagnosed with AIDS in December 1987 and in December 1988, as reported by the CDC. The authors’ estimate of the number of cases of AIDS in 1992 was determined in the same way using CDC data for December 1992 and for December 1993. Scitovsky and Rice estimated the nonpersonal costs of AIDS (including research, blood screening

and replacement, health education, information, and support services) in 1986 to be \$542 million, which is \$614 million in 1988 dollars inflated with the GDP medical care deflator. Hellinger determined the yearly costs of treating a person diagnosed with AIDS to be about \$60,000 in 1988. The product of this figure and the number of people diagnosed with AIDS who were alive in 1988 added to the Scitovsky and Rice estimate of the nonpersonal direct costs resulted in the authors' 1988 estimate. A similar procedure was used for the 1992 estimate, using data on the cost per case from a 1993 study. See Hellinger, F.J. The lifetime cost of treating a person with HIV. *Journal of the American Medical Association* (July 28, 1993) 270,4:474-78.

57. It has been estimated that, if the United States could have reduced its numbers of disabled low birth weight infants by one-half, the present value of the additional wages which those children could have earned over their lifetime would have been \$0.9 to \$1.9 billion in 1985. (Chu, R.C. *1985 indirect costs of infant mortality and low birth weight*. Washington, DC: National Commission to Prevent Infant Mortality, May 20, 1988.)

The Role of Basic Science in Preventing Low Birth Weight

Peter W. Nathanielsz

Abstract

Recent experimental studies in a wide range of animal species have shown that the fetus determines the duration of pregnancy. The mechanism by which the birth process is initiated is closely linked to the normal maturation of vital fetal organs, such as the lungs. Thus, under normal circumstances, the fetus should be adequately prepared for the challenges of an independent life after birth. The fetal endocrine changes that lead to birth result in increased maternal estrogen production and stimulation of effective uterine contractility and dilation of the cervix. Preterm delivery can occur as a result of several different pathological processes, including infection and various forms of stress. Successful strategies for preventing the preterm delivery of low birth weight infants will depend upon an improved ability to diagnose which of the many components of the normal birth process has been prematurely activated in each pregnant patient undergoing premature labor.

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Preterm labor occurs in approximately 10% of all pregnancies in the United States, and yet it gives rise to 75% of perinatal mortality.¹ The challenge for basic science is to understand the mechanisms that lead to normal delivery at the end of a normal pregnancy and to determine the critical points at which abnormal situations may precipitate preterm delivery of babies that have not reached their full birth weight and full maturation. In the past 20 years, considerable advances have been made in identifying the significant regulators of normal fetal growth and development. A clear picture has emerged from experimental studies on animals of how normal growth and maturation are linked and matched to the processes which initiate labor and delivery. A vast body of knowledge is available describing the genetic, cellular, tissue, and organ system functions that are responsible for normal fetal growth and the regulation of the birthing process.

One clear outcome of research in the past 20 years is the understanding that the birth process is a complex multifactorial system of interconnected physiological mechanisms. In addition, we shall see that preparatory changes in both mother and fetus occur several weeks before delivery. The birth process viewed in its entirety is not as sudden and dramatic as the final stages make us initially believe. The slower build up to birth that we have demonstrated in our studies on nonhuman pri-

mates and describe below is likely to assist the baby in her or his transition from the intrauterine environment to the new world outside. The complexities of hormonal regulatory mechanisms such as the endocrine and local paracrine systems will need to be unraveled in studies using animal models because a combination of simple observational studies and invasive or destructive procedures is required to provide a clear understanding of the birth process. In many instances, it would be unethical to conduct such experiments in humans because some of these experiments require procedures that inflict irreversible damage. Thus, precise knowledge

Experimental studies have demonstrated a very close link between normal birth timing and normal fetal growth.

of the normal processes of birth will come only from the study of normal birth in healthy nonhuman animal models. Studies on humans are of use in determining what goes wrong, but this clinical information needs to be evaluated against a background of clear knowledge of normal birth.

Many experimental studies have demonstrated that there is a very close link between normal birth timing and normal fetal growth. Thus, it has been suggested that somehow the fetus, and possibly the placenta, is able to monitor the baby's weight as an index of normal progress through the maturational process of gestation.² Algorithms and mathematical equations have been developed to describe the relationship between the baby's weight and the duration of pregnancy in many species. The purpose of this article is to describe the current level of understanding and interpretation of the available data about the mechanisms that initiate term and preterm birth.

Models for the Study of Normal Fetal Maturation

As a result of extensive use of selected and appropriate pregnant animal models to study both maternal and fetal development, a firm picture has developed over the past 20 years of normal fetal and maternal physiology. Extensive studies, particularly in pregnant sheep, have identified the factors that are responsible

for growth of the body as a whole and of specific vital organs such as the lungs, liver, gut, kidneys, and endocrine glands. For example, it has been demonstrated that, under normal circumstances, the fetus is undergoing periodic respiratory activity.³ The breathing patterns of the fetus in the uterus are episodic. Unlike adults, who need to breathe continuously to obtain their oxygen, the fetus is breathing only for practice. Fetal breathing movements have been shown to be necessary to develop the neuromuscular mechanisms in the brain and chest that will be vital for the newborn baby to take its first breath and maintain adequate respiration. In addition, breathing movements play a role in the development of the tissue of the lung itself.⁴ It is, therefore, important that the correct patterns of breathing have occurred in the uterus and that the baby has spent the correct amount of time in the uterus for the lungs to have reached their full developmental capacity before the time of birth.

This development of the lung, in part regulated by fetal breathing, is an excellent example of activity-dependent maturation. Activity of many development processes within the uterus plays a central role in normal development. If these processes are incomplete, inadequate, or truncated, then there may be long-term consequences for the individual. Many other examples of such activity-dependent maturation have been developed from studying fetal animals throughout pregnancy. One of the potentially most important is the demonstration of activity-dependent mechanisms in the central nervous system. Thus, normal development of the visual cortex of the brain depends on the arrival of appropriate neural information from the retina.⁵

In studies with pregnant sheep, it is possible to introduce a wide variety of challenges that simulate pathological situations which may affect the fetus in the uterus. Using sensors, it is possible to observe the response of the fetus. For example, during normal pregnancy, the fetus will respond to oxygen lack by redistributing its blood to its developing brain, heart, placenta, and adrenal glands. The fetus will protect these vital organs at the expense of reducing blood supply to the skin, gut, and other tissues which are not of immediate importance for survival.⁶ If blood supply to the fetal gut has been restricted for lengthy periods during fetal development, there is a likelihood that the

gut will be abnormally developed or may even die. Thus, protective mechanisms when utilized excessively can precipitate postnatal problems such as intestinal atresias or limb reduction defects. The ability of the fetus to compensate for a vast number of insults is a fundamental underlying concept of fetal development. However, animal studies have demonstrated that this protective compensatory mechanism can sometimes carry a price.

Although the sheep has been the pre-eminent animal model used to study development of the fetus in the uterus, much information has been obtained in other species including rats, guinea pigs, and nonhuman primates. As we shall see below, the information obtained clearly demonstrates the important commonalities among animal species in the processes of birth. In addition, studies on the regulation of uterine muscle contractility and the molecular biology of cellular mechanisms regulating growth and development have greatly advanced our knowledge in recent years.

Normal Fetal Growth

Normal fetal growth occurs when the fetus attains the appropriate and optimal size for his or her genotype. Growth in the uterus is a balance between the genetic potential of each individual fetus and the maternal environment. The intrauterine environment has been demonstrated to be a major factor in potentially restricting the genetic capability of the developing fetus. From the point of view of human pathophysiology, it follows that attention to the improvement of the intrauterine environment is a critical focus for better prenatal health care.

Optimizing the intrauterine environment for every baby will optimize that baby's growth. The classic study that demonstrated the importance of the intrauterine environment as a restrictor of genetic growth potential was performed in horses. In horses it is possible to conduct experiments in which large shire horses and small ponies are crossbred. Foals of crosses in which the large horse is the mother and the small pony the father are larger than the foals of the reverse cross, small pony mother and large shire horse father.⁷ These studies show that the maternal environment can constrain the full-growth potential.

Maternal nutrition is a major factor affecting fetal growth. During develop-

ment the fetus is given preferential access to many important nutrients, potentially acting as a drain on the mother. If the mother's health and nutritional intake are well balanced, this is usually no problem for the mother. However, when there is a shortage of nutrients, the fetus begins to compete for materials that are in short supply for its mother. Nature has so arranged things that the next generation has a powerful say in how the mother's nutrients are used in times of shortage. Regu-

Growth in the uterus is a balance between the genetic potential of each individual fetus and the maternal environment.

latory mechanisms exist which ensure that the mother's brain is well protected. However, next to the needs of the mother's brain, the needs of the fetus come second. There are many maternal and fetal regulatory systems which ensure that, after the maternal brain, the fetus is the last to suffer from any shortages. This protection of the fetus has been demonstrated in famine situations during wartime. The birth weight of babies can be seen to be remarkably well maintained even in prolonged famine such as occurred in Holland during World War II. In these extreme situations, fetal growth was affected only when there was pronounced dietary restriction during the third trimester.⁸ Much further work is needed before we can fully understand the effects of nutritional deficiencies and the maternal and fetal compensatory mechanisms used to combat them.

Mechanisms of Labor and Delivery

Maintenance of Pregnancy

Nature has developed a precise program that controls a baby's development in the uterus. During the 40 weeks of pregnancy, many vital systems must mature to an independent state.

The maintenance of a normal pregnancy for around nine months represents the balance of several maternal and fetal nutritional, hormonal, and immunological systems. The fetus is tolerated by the mother as it grows and matures according to a precisely scheduled program. Several

considerations suggest that the mother's body would normally want to reject this foreign invader. The fetus has its own distinct genetic composition which differs from that of the mother. Thus, the normal response of the mother's immune system should be to reject the fetus, but this does not happen. High concentrations of the hormone progesterone in the mother's blood quiet the spontaneous contractile activity of the uterine muscle. Pregnancy allows time for the baby to grow and mature, and for the mother to adjust her physiology to the needs of pregnancy. Before either normal term or preterm birth can take place, the factors that have maintained the pregnancy for nine long months must be overcome.

Correct timing of birth is necessary because the process of passing from the uterus to the outside world is far from being straightforward. The fetus has to make enormously complicated adjustments to its life-support systems in the very short space of time during which it moves

and pregnant animals to point researchers in the right direction to solve the mystery of the fetal role in the initiation of birth. In 1933, Percy Malpas, an obstetrician, wrote a medical-scientific paper describing the prolongation of human pregnancy that occurs when a fetus is born with part of the brain missing or deformed (anencephaly).⁹ In the anencephalic fetus, the front portions of the brain have failed to develop and the baby is generally born dead. If the anencephalic baby survives birth, it can live only a few hours without the support derived from the mother through the placenta. Unless other complications are present, anencephalic babies are generally born well past the normal expected time of birth. Some researchers took this as the first clue that the critical signals that start the process of birth might have been missing because they were lodged in the part of the fetal brain that was itself missing in the anencephalic baby.

In the early 1960s, reports began to circulate in the western United States regarding three related naturally occurring situations, two in cows and one in sheep, in each of which the duration of pregnancy was altered. In each instance, there were similar abnormalities in the fetal brain and fetal endocrine system that involved the hypothalamus and the pituitary.¹⁰ The hypothalamus regulates the pituitary by secreting a hormone, corticotropin-releasing hormone (CRH). CRH stimulates the pituitary to secrete adrenocorticotropin (ACTH). ACTH is a hormone which regulates how much of another hormone, cortisol, is secreted by the adrenal cortex. Cortisol regulates the function of several different tissues. Any of these steps can provide opportunities for control of the whole system taken together. They are also a potential cascade that permits rapid and pronounced amplification of the system (see Figure 1).¹¹

Pregnant sheep who have eaten the corn lily plant, common in the western states, have been known to carry their lambs well past 200 days of pregnancy. This degree of prolongation of pregnancy is remarkable because sheep normally give birth after about 150 days of pregnancy. The fetal lambs of ewes who had eaten the corn lily were not born. They had to be removed surgically from the ewes by cesarean section. Some of these fetal lambs had not been born even as late as 250 days of pregnancy. A pregnancy lasting 250

Pregnancy allows time for the baby to grow and mature, and for the mother to adjust her physiology to the needs of pregnancy.

from a fetal condition to that of a newborn baby. Having overcome the challenges of normal development in the uterus, the fetus must use several previously untried organ systems to survive in a completely different environment. The timing of initial exposure to these new challenges is critical for its survival.

The Role of the Fetus in Initiating the Birth Process

The Greek philosopher, physician, and scientist Hippocrates, who lived in the fifth century B.C., firmly believed that the baby decides when the birth process will begin. He said, "When the child has grown big and the mother can no longer support him with food, he struggles and breaks forth into the world, free from all bonds." Hippocrates held strongly to the view that the signal that begins the process is a failure of the placenta to keep up with the increasing nutritional needs of the fetus.

It took the observation of unusual disease conditions in both pregnant women

Figure 1

days in sheep is equivalent to a human pregnancy lasting 15 months instead of the normal 9 months. The affected lamb fetuses had brain deformities involving the hypothalamus and pituitary. Detailed chemical analysis proved that these deformities were caused by one specific toxic compound in the plant. If the embryo was at a critical point of its development when the plant was eaten, the fetal brain developed abnormally. Studies proved that the toxic compound has to reach the fetal brain on the 14th day of pregnancy.¹⁰

These and many other observations of prolonged pregnancy have one underlying theme. They all suggest a critical role for the fetal hypothalamus, pituitary, and adrenal gland in the process of birth (see Figure 1).¹¹

Controlled experimental studies of the brain were begun in the late 1960s. Mont (G.C.) Liggins, an obstetrician from New Zealand, removed the pituitary gland from fetal sheep at around 115 days of pregnancy. In the absence of normal function of the pituitary gland of the fetus, pregnancy went on well past its normal length of 150 days. In separate studies, he found that removal of both of the fetal adrenal glands from fetal sheep also led to prolongation of pregnancy. Professor Liggins reasoned that, if he reversed the process and stimulated premature growth of the adrenal of the fetal lamb while it was still in the uterus, the duration of the pregnancy would be shortened. At 120 days of pregnancy he infused a fetal lamb which was still in the uterus with ACTH to cause

the fetal adrenal glands to grow prematurely. The lamb was born within four days. If Professor Liggins bypassed a step in the birth process and infused fetal lambs with cortisol, which is the major product of the adrenal gland, the lambs were born in three days. Fetal lambs infused with saline, which he used as a control experiment, did not deliver early; they remained in the uterus and were born at the correct time, around 150 days of pregnancy. These elegant studies firmly established that, in the sheep, the fetus is the originator of the signal to be born. The studies also clearly established the fetal pituitary and adrenal system as the major pathway for the signals that initiate the birth process.¹²

Fetal Control of Lung Maturation

These elegant studies yielded unexpected observations of extreme importance. Lambs born at 125 days of pregnancy following infusion of ACTH or cortisol into their blood were able to breathe normally. In contrast, the lungs of the control lambs infused with saline and delivered at the same time were too immature to survive. It was immediately apparent that the same hormones produced by the fetus that initiate birth are also key factors in the literally vital development of the fetal lung for air breathing after birth.

As a result of increased activity of the fetal brain, the fetus secretes more ACTH and cortisol, producing the changes that lead to birth.

As a direct result of this observation, a series of elegant studies was commenced that led to the current policy of treating mothers in preterm labor with steroids so that fetal lung maturation can be accelerated and the baby has a better chance of survival if born preterm.¹³ (See the article by Ricciotti in this journal issue which discusses the use of steroids in human pregnancies.) This elegant series of studies, designed to determine the critical factors that regulate the duration of pregnancy and match it with normal fetal maturation, is an excellent example of the value of basic science research and the use of animal models to unlock the secrets of fetal development and lead to better clinical care of the immature preterm baby.

The Controlling Function of the Fetal Brain

The production of ACTH in the fetal lamb is controlled by CRH from the fetal brain. This hormone is secreted by two paraventricular nuclei, small collections of nerve cells each about the size of a ball bearing, one on either side of the fetal hypothalamus. Recent studies at the College of Veterinary Medicine at Cornell University have concentrated on these nuclei. These studies, conducted by Dr. Thomas McDonald and the author, have shown that, if radio frequency waves are used experimentally to destroy both of these nuclei in the fetal hypothalamus at 120 days of pregnancy, the pregnancy is prolonged.¹⁴

There is now a firm body of experimental evidence to show that late in pregnancy, about 20 days before birth, the fetal lamb pituitary gland begins to increase its secretion of ACTH, stimulating the fetal adrenal cortex to grow and to secrete more cortisol. Neither ACTH nor cortisol in the blood of the pregnant ewe crosses the placenta easily. Consequently, the fetal adrenal gland is protected from the effects of changes in maternal ACTH which may occur as a result of maternal stress. Although in human pregnancy ACTH will not cross the placenta, adrenal steroids can cross the placenta from the mother to the fetus.¹⁵ Thus, because this protection of the fetus from hormonal changes in the mother may be less effective in humans, it may explain some types of preterm birth.

Linkage of Fetal and Maternal Hormone Action to Uterine Contraction

Taken together, the series of studies in pregnant sheep shows that, as a result of increased activity of the fetal brain, the fetus secretes more ACTH and cortisol, producing the changes that lead to birth. The muscle layers of the uterus (the myometrium) are regulated by both inhibitory and stimulatory molecules. During pregnancy the balance is in favor of inhibition of uterine contraction so that the pregnancy will be maintained. At the end of pregnancy, so that birth may occur, the balance of regulatory factors that control the myometrium has to be switched to stimulation.

In sheep and other species, the hormone progesterone has an inhibitory effect on the uterine muscles. In contrast, estrogens are stimulatory to the uterine muscles. As the blood from the fetal lamb

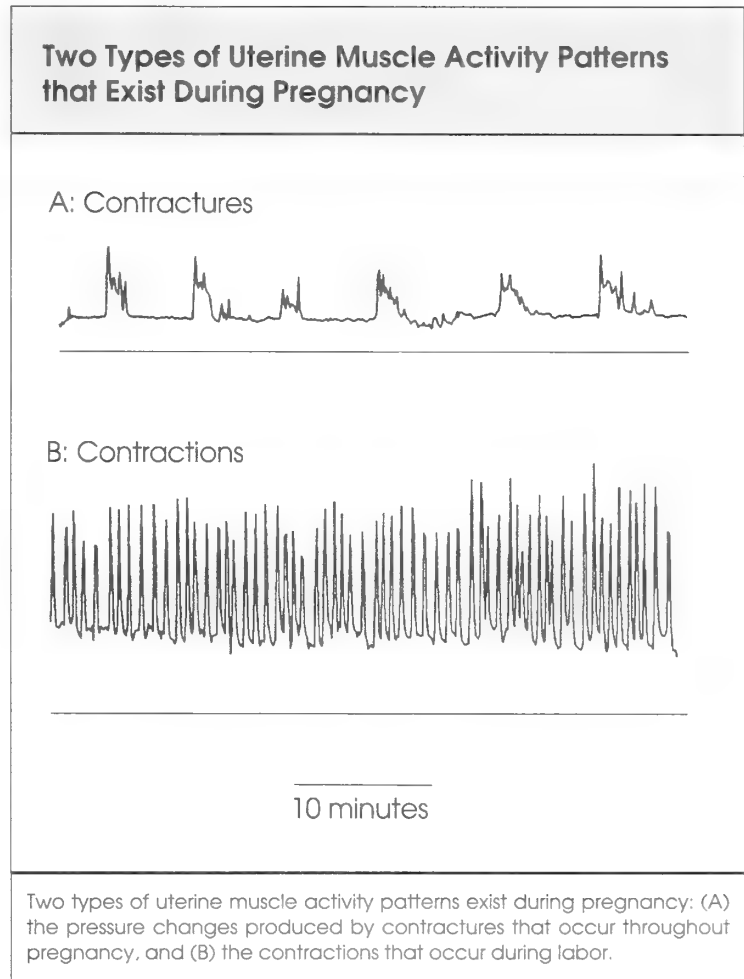
passes through the placenta, cortisol in the fetal blood stimulates the placenta to produce enzymes that convert progesterone molecules into estrogens. This fall in progesterone level and associated rise in estrogen production is the first step in a precisely timed cascade of effects.¹⁶ As progesterone production by the placenta falls and estrogen production rises, the balance that has kept the uterine muscle relatively quiet throughout pregnancy begins to change in favor of the stimulatory group of steroids, the estrogens. These and other associated hormone changes in the mother will stimulate the uterus to contract.

Different Types of Uterine Activity—Contractures and Contractions

In 1872, Braxton Hicks described long-lasting contractions of the pregnant uterus throughout pregnancy in women. Experimental studies in a large number of animal species have shown that low-intensity episodes of uterine muscle activity lasting as long as 10 minutes occur throughout pregnancy. To distinguish this type of activity from labor and delivery contractions, from which they are very different, we have called these epochs of activity “contractures” (see Figure 2).

In the pregnant sheep, a series of events occurs to alter the hormonal balance which results in the initiation of labor. The concentration of progesterone in the mother's blood falls over the final three to four days of pregnancy, and with this change, labor is initiated. Simultaneously, maternal plasma estrogen concentrations rise.¹⁷ Estrogen stimulates the production of several other hormones (such as oxytocin) and regulatory compounds that also stimulate uterine contractions. Estrogen also stimulates production of more oxytocin receptors on the surface of the muscle cells of the uterus, thereby stimulating them to contract more strongly and regularly.¹⁸ While estrogen is classically considered to exert all its effects as a hormone, accessing target tissues via the blood, it now appears that some of its actions may depend on local, cell-to-cell interactions. Local regulatory compounds are also produced within the lining of the uterus. The most important of these are prostaglandins, which act in concert with oxytocin. The final result of these maternal hormonal and paracrine changes is to produce a dramatic switch of contractures to contractions.¹⁹

Figure 2



Source: Nathanielsz, P.W. A time to be born. In *Life before birth and a time to be born*. Ithaca, NY: Promethean, 1992. Reprinted with permission.

The Role of the Cervix

Throughout pregnancy the cervix has acted as a tight constriction at the opening of the uterus, helping to keep the fetus in the uterus. A popular fallacy is that the cervix is a muscle that is tightly contracted to prevent the premature departure of the baby from the uterus. The normal cervix is a tough, unyielding collection of fibrous tissue strands. The strands are made up of long threadlike molecules strongly bound to each other. Because the cervix is generally tightly closed, it also acts to prevent the passage of infectious agents from the vagina into the uterus. Infection is now considered one of the major causes of preterm birth.²⁰

In the vast majority of pregnancies, the cervix remains tightly closed until the last three to four weeks of pregnancy, when it begins to soften in preparation for dilation during the birth process. This early soften-

ing begins as a very gradual process that takes place over several days. Prostaglandin production, probably within the cervix itself, plays a key role in the cervical dilation and softening process.²¹ As we have seen, prostaglandin production is strongly regulated by estrogen so, under normal circumstances, the key processes that lead to birth are closely interlocked and, ultimately, controlled by the initial signals sent out by the fetus.

The uterus is a muscular bag, similar in many ways to the heart. Both are beyond conscious control. There is nothing anyone can do to influence the operation of either the heart or the uterus as a conscious act of will: they are involuntary mus-

Prostaglandin production, probably within the cervix itself, plays a key role in the cervical dilation and softening process.

cles. Although there are differences, the fine structure of the individual muscle cells is similar in the heart, the digestive system, and the uterus. On the other hand, uterine muscle cells are very different from the cells in muscles such as those of the limbs that can be moved voluntarily as a conscious act of will. The wall of the uterus contains two major sheets of involuntary muscle; one that is orientated in a circular fashion around the uterus and one that is placed longitudinally around the uterus. When the longitudinal muscle contracts, the uterus shortens and the fetus is driven through the cervix, providing that the cervix is adequately dilated. Contraction of both of these layers of uterine muscle is completely involuntary. A pregnant woman cannot consciously control the contraction of her uterus just as she cannot consciously control the beating of her heart or the activity of her stomach.

Several of these regulatory molecules alter the contractile properties of uterine muscle. As we have seen, progesterone, a steroid hormone like many of the molecules involved in the process of birth, has inhibitory effects on uterine muscle contraction. Acting in opposition to progesterone, estrogens stimulate uterine muscle contractility. They do so, in part, by instructing the lining of the uterus (the decidua) to increase the production of prostaglandins, which are local regulatory

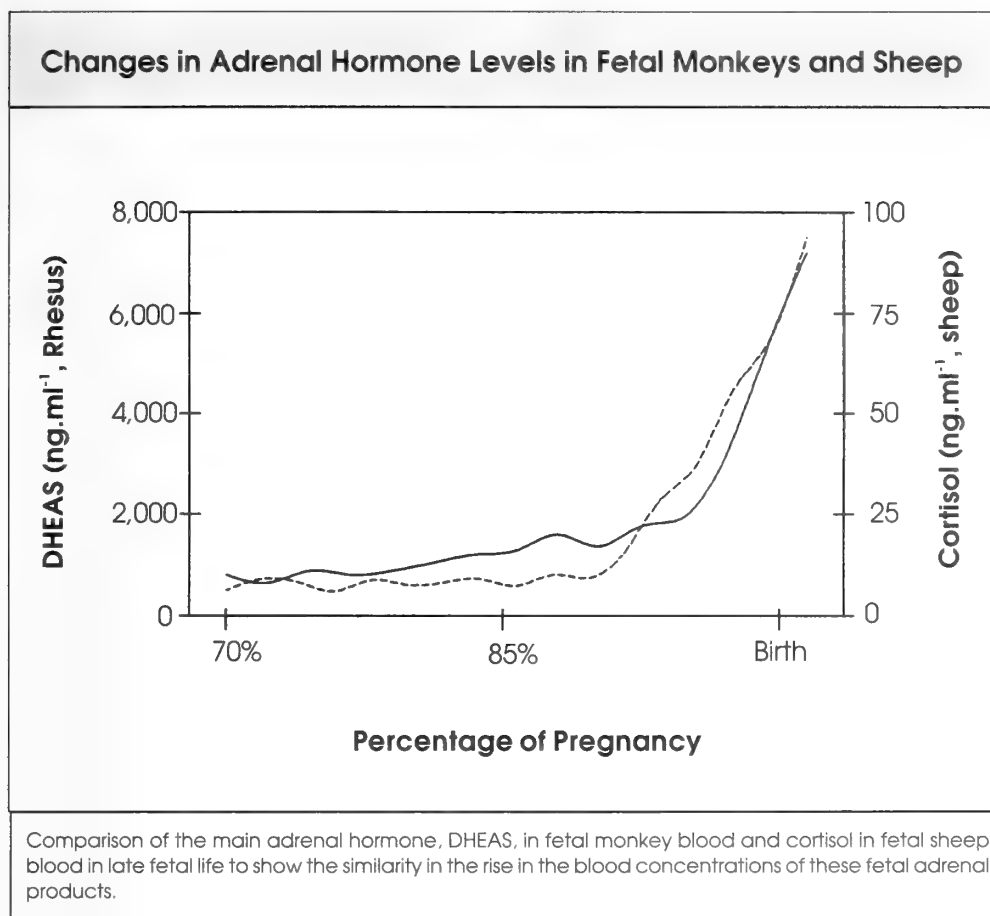
compounds.²² The prostaglandins diffuse from cells of the decidua to the muscle cells beneath it and stimulate them to contract. The level, type, and pattern of uterine muscle contraction is determined by the balance of factors that tend to keep the uterine muscle relatively inactive and the factors that tend to stimulate activity. Maintenance of a normal pregnancy for its full duration requires the balance to be in favor of the inhibitory factors. At birth, the regulatory balance is tilted in favor of stimulation of the muscle of the uterus. At this time the muscle switches from the irregular, weak pattern of activity it has been undergoing throughout pregnancy to strong, well-coordinated labor contractions. The change in circulating hormones and paracrine regulators also causes the cervix to dilate.

Experimental Studies in Nonhuman Primates

Most of the evidence that has helped to explain the regulation of labor comes from experimental work on sheep. However, several studies indicate that the mechanisms are similar in primates, including pregnant women. Two lines of evidence from studies conducted on monkeys suggest that mechanisms similar to those so carefully and clearly shown in fetal sheep are also important in initiating normal birth at the end of normal pregnancy in nonhuman primates. In the last 10% of the time the sheep fetus spends in the uterus, the fetal adrenal begins to secrete more and more cortisol into his blood until, at delivery, the concentration of cortisol in fetal blood has risen to levels 20 times those present 15 days before birth. As mentioned above, cortisol stimulates more estrogen to be produced and less progesterone by the placenta, changing the balance of factors regulating the level of contraction of the uterine muscle.

By a different route the monkey does much the same thing. The fetal monkey adrenal predominantly secretes the steroid dehydroepiandrosterone sulfate (DHEAS). DHEAS is converted to estrogen in the placenta. If we draw a graph of the rise in cortisol in the blood of the fetal sheep in late pregnancy and superimpose on this graph the rise in DHEAS in fetal monkey blood over the same portion of pregnancy, the lines are virtually identical (see Figure 3). The strategy of the two species is slightly different, but the end product is the same. The fetal monkey instructs his adrenal glands to produce

Figure 3



Source: Nathanielsz, P.W. A time to be born. In *Life before birth and a time to be born*. Ithaca, NY: Promethean, 1992. Reprinted with permission.

precursors, or building blocks, from which the cells in the placenta can make estrogen.²³ The fetal sheep, on the other hand, uses cortisol to produce enzymes in the placenta which convert progesterone to estrogen. In both species estrogen enhances the effect of the oxytocin which is produced by the mother, stimulating prostaglandin production and leading to an enhanced ability of the uterine muscle to contract. The overriding point of importance is that in both species it is the fetal brain, through the mechanism of the hypothalamo-hypophyseal-adrenal axis, that plays the fundamental role in deciding the length of pregnancy.²²

Rhythms in the Switch from Contractures to Contractions in Pregnant Primates, Including Pregnant Women

A better understanding of both normal term and preterm birth must address the interesting observation that labor begins more frequently at nighttime than during

the daytime.²⁴ It is important to understand the maternal and fetal mechanism responsible for this pattern. Several investigators have shown that there are pronounced 24-hour rhythms in maternal hormone concentrations, including estrogen and oxytocin in both pregnant women^{25,26} and pregnant nonhuman primates.^{27,28} These rhythms are driven by the circadian clock in the mother's brain. The significance of these rhythms lies in the potential to effectively restrict therapies and interventions to the time of the day at which they are likely to be most needed and most successful. It has been shown that maternal plasma oxytocin concentrations increase in the late evening hours. It would thus seem appropriate to investigate the effectiveness of prophylactic therapies with oxytocin antagonists administered in the mid to late afternoon.

Pathological Processes

The purpose of this review has been to describe the functional systems involved in

normal birth at the end of a pregnancy of normal duration. A better understanding of these mechanisms will permit determination of the pathological modification of the process that leads to preterm birth. The pathological modifications that may result in preterm delivery are diverse. One simple mechanical feature that can lead to

maternal estrogens may then prematurely activate the switch from contractures to contractions.³⁰

Maternal Lifestyle

The many stresses that assail us in modern life may be amplified for the pregnant woman. We have seen that activation of the maternal adrenal can produce the same hormones, normally produced by the fetus, that initiate birth at the end of a normal pregnancy. In addition, many of the common maternal behavioral responses to stress, smoking tobacco, drinking alcohol, and even taking prescription drugs may adversely affect the fetus, thereby possibly stimulating the baby to release the same adrenal hormones. It is also possible that other stresses, such as financial worry, excessive physical exertion, and poor nutrition, may have the potential to prematurely activate the cascade of maternal and fetal hormones that switch contractures to contractions and cause dilation of the cervix. At present, we have little knowledge about what actually causes preterm labor, and additional attention to maternal lifestyle may provide new clues about the initiation and cause of preterm labor.

Experimental Agents Used to Study Prevention of Preterm Birth

Several new drugs are being tested which have the potential to suppress uterine contractions and, thus, to prevent preterm birth. A brief discussion of the most promising drugs is presented below. Further discussion of the uses of these drugs in clinical practice is included in the article by Ricciotti and colleagues in this journal issue. While many of these drugs are authorized for clinical use, they generally have not proven to be highly successful in suppressing contractions for more than one or two days, and many have very serious side effects for both the mother and the fetus.

Oxytocin Antagonists

The improvement of our understanding of the role of oxytocin in the birth process has led to increased interest in the potential use of oxytocin antagonists in the prevention and treatment of preterm labor. In nonhuman primates, these antagonists possess a very powerful ability to switch the contractile pattern of the uterus back from the ominous labor-threatening contractions mode to the innocuous, contractures mode that is the characteristic pattern throughout pregnancy.²⁸ At least one oxy-

At present, we have little knowledge about what actually causes preterm labor.

preterm delivery is a structural abnormality of the cervix. Other causes of preterm birth are more complex and less well understood. Two major causes merit consideration. These are infection and maternal stress.

Infection is now considered to be responsible for somewhere between one-third and one-half of all preterm births. Infectious organisms release toxins that trigger responses from the immune system of the host animal.²⁰ Toxins released from low-grade local infections within the pregnant woman's reproductive tract or, perhaps less commonly, from infections in other organs in the mother's body will stimulate her immune system to produce a wide variety of very active compounds, many of which, including the prostaglandins, are normally used to bring about the switch from contractures to contractions and dilation of the cervix that normally occur at term. Further studies are required to understand the key mechanisms stimulated by infection and to develop drugs to inhibit them. The best treatment is, however, to prevent these infections by improving maternal health.

Many epidemiological studies have demonstrated that a variety of maternal stress situations are correlated with an increased incidence of low birth weight.²⁹ Some of these are discussed elsewhere within this journal issue. It is likely that several functional systems whose activity is increased during maternal stress are involved in the greater tendency of the pattern of uterine contractility to switch from contractures to contractions. Maternal stress will activate the maternal adrenal cortex and result in increased secretion of androgen, which is the immediate precursor for estrogen production. Increased

tocin antagonist is currently being tested in human clinical trials, and early results are promising. However, it must be remembered that the causes of preterm labor are many and that some of them, especially infection, may precipitate preterm labor as a result of increased prostaglandin synthesis. Thus, in this situation the most rational approach is to treat both the infection and the increased prostaglandin production, although oxytocin antagonists may help by inhibiting the recruitment of oxytocin's action during the responses to infection.

Inhibitors of Prostaglandin Synthesis

Powerful inhibitors of the production of prostaglandins have been used in management of preterm labor with some success. However, the agents that act in this manner which are currently available will cross the placenta and may have marked effects on fetal breathing, renal function, and circulation.³¹

Drugs that Affect the Sympathetic Nervous System

The only agents that have been authorized for general clinical use to inhibit preterm uterine contractility activity are the betamimetic drugs. These compounds have been shown to inhibit uterine contraction.³² However, these agents do have maternal side effects such as increased heart rate and retention of fluid. They also have limited efficacy, lasting for only 24 to 48 hours. In animal experimental studies, it has been shown that long-term administration of betamimetic drugs may stimulate prostaglandin secretion³³ and may, therefore, have the ability to augment the processes that are leading to preterm labor. Much more research is needed to determine exactly how these compounds and other agents work to prevent preterm birth.

Calcium Channel Blockers

Because an increase in intracellular calcium is probably the fundamental mechanism that causes contraction of uterine smooth muscle, agents have been developed which inhibit the passage of calcium into the cell both from the outside fluids bathing the cells and also from stores within the cell itself. These agents have a strong effect on uterine smooth muscle; however, they have pronounced effects on other tissues as well.³⁴ They must be used with considerable caution, and an ample amount of future research is required.³⁴

Future Research Needs

This review has highlighted the enormous advances in our understanding of normal term labor. A clear sequence of physiological events has been demonstrated which shows that the fetus determines the time to be born by sending hormonal signals to the brain from the placenta. Similar mechanisms are responsible for the onset of labor in primates as well as ruminants and probably all other species born at an advanced level of maturation. Other mechanisms may occur in species such as the rat. In species where there are multiple fetuses born at a much lower level of maturity, other strategies are employed. However, the concept that the fetus, under normal circumstances, determines the timing of delivery by means of systems and processes similar to those used to mature vital fetal organs is extremely important. These systems and processes tend to prevent a mismatch between the timing of delivery and the maturation of vital fetal organs. The primary problem is to understand the mechanisms of preterm birth. The first thing that must be clearly stated

A clear sequence of physiological events has been demonstrated which shows that the fetus determines the time to be born.

is that preterm birth has many causes. Thus, therapies will require a variety of approaches. A clearer understanding of the mechanisms of preterm labor is essential to the design of new agents to inhibit its occurrence.

Specifically, further research needs to be conducted on the origin and nature of the signals in the fetal brain that begin the process leading to activation of the fetal adrenal cortex in primates and the linkage of this signal to the switch of myometrial activity from contractures to contractions. It is necessary to understand the regulation of this repeating switch and its final representation as the strong rhythmic contractions stimulated by several different hormones linked to each other by feed forward controls. Finally, it is necessary to determine the extent to which the changes that occur at normal term birth are recruited prematurely during preterm birth and the extent to which abnormal mecha-

nisms that do not occur in normal term delivery are responsible for the preterm birth of low birth weight babies. One area of key importance is the relationship between growth retardation and preterm birth. While there is evidence that growth retardation is associated with preterm birth,^{35–38} the mechanisms involved are

retardation while, at the same time, stimulating the birthing process and prematurity that may arise because the stressed, growth-retarded fetus has prematurely initiated labor. Clinical management of these two scenarios will differ considerably.

A clearer understanding of the mechanisms of preterm labor is essential to the design of new agents to inhibit its occurrence.

unclear. It is vitally important to be able to differentiate between types of prematurity in which the pathology leads to growth

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1. Creasy, R.K. Preterm labor and delivery. In *Maternal-fetal medicine: Principles and practice*. 2d ed. R.K. Creasy and R. Resnik, eds. Philadelphia: W.B. Saunders, 1989, pp. 477–504.
2. Hofman, M.A. Evolution of brain size in neonatal and adult placental mammals: A theoretical approach. *Journal of Theoretical Biology* (1983) 105:317–32.
3. Dawes, G.S. The rediscovery of fetal breathing movements and its consequences. In *Respiratory control and lung development in the fetus and newborn*. B.M. Johnston and P.D. Gluckman, eds. Ithaca, NY: Perinatology Press, 1986, pp. 209–22.
4. Gross, I. The biochemical development of fetal lung. In *Respiratory control and lung development in the fetus and newborn*. B.M. Johnston and P.D. Gluckman, eds. Ithaca, NY: Perinatology Press, 1986, pp. 87–105.
5. Rakic, P., and Riley, K.P. Regulation of axon number in primate optic nerve by perinatal binocular competition. *Nature* (1983) 305:135–37; Rakic, P. Specification of cerebral cortical areas. *Science* (1988) 241:170–76.
6. Peeters, L.L., Sheldon, R.E., Jones, Jr., M.D., et al. Blood flow to fetal organs as a function of arterial oxygen content. *American Journal of Obstetrics and Gynecology* (1979) 135:637–46.
7. Walton, A., and Hammond, J. The maternal effects on growth and conformation in the shire-horse-Shetland pony cross. *Proceedings—Royal Society of Edinburgh. Section B: Biology* (1938) 125:311.
8. Stein, Z., and Susser, M. The Dutch Famine, 1944–1945, and the reproductive process. I. Effects on six indices at birth. *Pediatric Research* (1975) 9:70–76.
9. Malpas, P. Postmaturity and malformations of the foetus. *Journal of Obstetrics and Gynaecology of the British Commonwealth* (1933) 40:1046–53.
10. Binns, W., Shupe, J.L., Keeler, R.F., and James, L.F. Chronologic evaluation of teratogenicity in sheep fed veratrum californicum. *Journal of the American Veterinary Medical Association* (1965) 147:839–42.
11. Nathanielsz, P.W. A time to be born. In *Life before birth and a time to be born*. Ithaca, NY: Promethean, 1992, pp. 162–81.
12. Liggins, G.C., Fairclough, R.J., Grieves, S.A., et al. The mechanism of initiation of parturition in the ewe. *Recent Progress in Hormone Research* (1973) 29:111–49.
13. Liggins, G.C., and Howie, R.N. A controlled trial of antepartum glucocorticoid treatment for prevention of the respiratory distress syndrome in premature infants. *Pediatrics* (1972) 50:515–25.
14. McDonald, T.J., and Nathanielsz, P.W. Bilateral destruction of the fetal paraventricular nuclei prolongs gestation in sheep. *American Journal of Obstetrics and Gynecology* (1991) 165:764–70.

15. Ducusay, C.A., Cook, M.J., Walsh, S.W., and Novy, M.J. Circadian patterns and dexamethasone-induced changes in uterine activity in pregnant rhesus monkeys. *American Journal of Obstetrics and Gynecology* (1983) 145:389-96.
16. Anderson, A.B.M., Flint, A.P.F., and Turnbull, A.C. Mechanism of action of glucocorticoids in induction of ovine parturition: Effect of placental steroid metabolism. *Journal of Endocrinology* (1975) 66:61-70.
17. Challis, J.R.G. Sharp increase in free circulating oestrogens immediately before parturition in sheep. *Nature* (1971) 229:208.
18. Fuchs, A., Periyasamy, S., Alexandrova, M., and Soloff, M. Correlation between oxytocin receptor concentration and responsiveness to oxytocin in pregnant rat myometrium: Effects of ovarian steroids. *Endocrinology* (1983) 113:742-49.
19. Taylor, N.F., Martin, M.C., Nathanielsz, P.W., and Seron-Ferre, M. The fetus determines circadian oscillation of myometrial electromyographic activity in the pregnant rhesus monkey. *American Journal of Obstetrics and Gynecology* (1983) 146:557-67.
20. Romero, R., Mazor, M., Wu, Y.K., et al. Infection in the pathogenesis of preterm labor. *Seminars in Perinatology* (1988) 12:262-79.
21. Fitzpatrick, R.J., and Liggins, G.C. Effects of prostaglandins on the cervix of pregnant women and sheep. In *Dilatation of the uterine cervix*. F. Naftolin and P.G. Stubblefield, eds. New York: Raven, 1980, pp. 287-300.
22. Challis, J.R.G., and Olson, D.M. Parturition. In *The physiology of reproduction*. E. Knobil and J.D. Neill, eds. New York: Raven, 1988, pp. 2177-216.
23. Siiteri, P.K., and Seron-Ferre, M. Some new thoughts on the fetoplacental unit and parturition in primates. In *Fetal endocrinology*. M.J. Novy and J.A. Resko, eds. New York: Academic Press, 1981, pp. 1-34.
24. Malek, J. The manifestation of biological rhythms in delivery. *Gynaecologia* (1952) 133:365-72.
25. Fuchs, A.R., Behrens, O., and Liu, H.C. Correlation of nocturnal increase in plasma oxytocin with a decrease in plasma estradiol/progesterone ratio in late pregnancy. *American Journal of Obstetrics and Gynecology* (1992) 167:1559-63.
26. Patrick, J., Challis, J., Campbell, K., et al. Circadian rhythms in maternal plasma cortisol and estradiol concentrations at 30 to 31, 34 to 35, and 38 to 39 weeks' gestational age. *American Journal of Obstetrics and Gynecology* (1980) 136:325-34.
27. Walsh, S.W., Stanczyk, F.Z., and Novy, M.J. Daily hormonal changes in the maternal, fetal, and amniotic fluid compartments before parturition in a primate species. *Journal of Clinical Endocrinology and Metabolism* (1984) 58:629-39.
28. Honnabier, M.B.O.M., Figueroa, J.P., Rivier, J., et al. Studies on the role of oxytocin in late pregnancy in the pregnant rhesus monkey: Plasma concentrations of oxytocin in the maternal circulation throughout the 24th day and the effect of the synthetic oxytocin antagonist [1-beta-Mpa(beta-(CH₂)₅)₁, (Me(Tyr₂, Orn₈) oxytocin on spontaneous nocturnal myometrial contractions. *Journal of Developmental Physiology* (1989) 12:225-33.
29. Kaminski, M., and Papiernik, E. Multifactorial study of the risk of prematurity at 32 weeks of gestation. *Journal of Perinatal Medicine* (1974) 2:37-44.
30. Figueroa, J.P., Honnabier, M.B.O.M., Binienda, Z., et al. Effect of 48 hour intravenous 4A androstenedione infusion on the pregnant rhesus monkey in the last third of gestation: Changes in maternal plasma estradiol concentrations and myometrial contractility. *American Journal of Obstetrics and Gynecology* (1989) 161:481-86.
31. Fuchs, F., and Stubblefield, P.G., eds. *Preterm birth: Causes, prevention, and management*. New York: Macmillan, 1984.
32. Canadian Preterm Labor Investigators Group. Treatment of preterm labor with the beta-andrenergic agonist ritodrine. *New England Journal of Medicine* (1992) 327:308-12.
33. Lye, S.J., Christopher, P., and Casper, R.F. Effects of B-adrenergic agonist infusions on myometrial activity and plasma prostaglandin levels in the nonpregnant sheep. *Canadian Journal of Physiology and Pharmacology* (1986) 65:2297-301.
34. Ducusay, C.A., Thompson, J.S., Wu, A.T., and Novy, M.J. Effects of calcium entry blocker (nicardipine) tocolysis in rhesus macaques: Fetal plasma concentrations and cardiorespiratory changes. *American Journal of Obstetrics and Gynecology* (1992) 157:1482-86.
35. Goldenberg, R.L., Nelson, K.G., Koski, J.F., and Cutter, G.R. Low birth weight, intrauterine growth retardation, and preterm delivery. *American Journal of Obstetrics and Gynecology* (1985) 152:980-84.

36. Weiner, C.P., Sabbagha, R.E., Vaisrub, N., and Depp, R. A hypothetical model suggesting suboptimal intrauterine growth in infants delivered preterm. *Obstetrics and Gynecology* (1985) 65:323.
37. Ott, W.J. Intrauterine growth retardation and premature delivery. *American Journal of Obstetrics and Gynecology* (1993) 168:1710–17.
38. Tamura, R.K., Sabbagha, R.E., Depp, R., et al. Diminished growth in fetuses born premature after spontaneous labor or rupture of membranes. *American Journal of Obstetrics and Gynecology* (1984) 148:1105.

The Role of Obstetrical Medical Technology in Preventing Low Birth Weight

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Abstract

Technology plays an important role in the practice of medicine, and it is essential that controlled clinical trials be conducted before new technologies are widely disseminated. In this article, information from the medical literature is summarized and critiqued for several common obstetric technologies which are aimed at reducing the incidence or sequelae of low birth weight and preterm birth. These technologies include home uterine activity monitoring, tocolytic drugs to suppress uterine contractions, corticosteroids to accelerate fetal lung maturity, bed rest to prevent preterm delivery, delivery methods, multifetal pregnancy reduction, and cervical cerclage. A major challenge to the practice of medicine is to find effective ways to modify physician behavior to encourage the use of proven, effective technologies, and discourage the use of unproven, ineffective technologies. Despite widespread use, most obstetrical technologies appear to have had little impact on reducing the incidence of low birth weight or preterm births, as rates of low birth weight and preterm birth have not decreased appreciably in the past 25 years. Uncovering the basic mechanisms responsible for the onset of preterm labor will undoubtedly facilitate the discovery of new technologies to prevent low birth weight and preterm births.

Obstetricians are very dependent on technology in their practice of medicine. Sophisticated machines are used to visualize and monitor physiologic signs of the fetus and the uterus; drugs and surgical procedures are often used to help reduce serious illnesses and prevent fetal deaths. But has the introduction of obstetric procedures and technologies had a measurable impact on reducing the incidence and sequelae of low birth weight or preterm birth?

While it is difficult to determine what proportion of preterm births might be prevented by obstetric technology, it is possible to evaluate these technologies to determine which of them actually improve birth outcomes. Unfortunately, as in other areas of medicine, many obstetrical tech-

nologies have been adopted despite the lack of evidence of their effectiveness in preventing death or illnesses. As a result, some common interventions make little or no difference in outcomes, and some may even be harmful. Conversely, several effective technologies are underutilized, and

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this underuse also causes harm. The purpose of this article is to evaluate the efficacy of several obstetric technologies related to preterm birth and to summarize the impact that obstetric technology has had on preventing the occurrence of low

As in other areas of medicine, many obstetrical technologies have been adopted despite the lack of evidence of their effectiveness in preventing death or illnesses.

birth weight or preterm births. We start by looking at the scientific evidence regarding several commonly used obstetric technologies and later discuss the overall impact that technology has on reducing infant deaths and preventing low birth weight births.

Home Uterine Activity Monitoring

Home uterine activity monitoring (HUAM) is a system of care that was introduced in an attempt to reduce the number of children born preterm. It couples use of

a monitoring device with daily nursing contact by phone to provide support and advice as to when a woman should go to the hospital. Women attach an external tocodynamometer (a device strapped over the abdomen which senses uterine contractions and records their frequency) twice a day for one to two hours while lying down. The recordings are then transmitted via telephone to a central station.

If contractions are deemed excessive (usually four to six contractions per hour is considered the upper limit of acceptability), the woman is advised to seek medical care. The monitoring equipment has generally been shown to detect uterine contractions accurately; however, this premise was questioned at a recent meeting at the Food and Drug Administration.¹ The approximate charge for the home uterine monitoring system is \$90 to \$100 per day. If the system is used between 24 and 36 weeks of gestation, the cost could easily exceed \$7,000 for each pregnancy.²

It is thought that use of the monitor will help to identify an increase in contractions which are not perceived by the woman. The increase in unfelt contractions is thought to signal the very beginning of the process of preterm labor. Drug

Figure 1

therapy aimed at stopping these contractions can then be given with the hope of preventing a preterm birth. It is not clear just how effective the monitors are in preventing preterm births because there have been no large-scale controlled scientific studies to determine their effectiveness.

Several studies of the monitor, which were conducted on a small number of women, concluded that it may be useful as an early warning system for preterm labor,^{3,4} but these studies have not determined whether the monitor or the daily nursing contacts that accompany it are responsible for the favorable results. Further studies have suggested that the daily nursing care was actually responsible for the improved birth outcomes, not the monitor.^{5,6} However, it appears that labor is detected slightly earlier if only the monitor is used.⁷ A recent review of this topic has indicated that all of the evaluations of this technology had serious methodologic deficiencies.⁸ Nonetheless, four of the five trials demonstrated no significant benefit from monitoring.

The American College of Obstetricians and Gynecologists recommends that home uterine activity monitoring devices remain investigational and not be routinely used.² The College concluded that, until the efficacy of the technology has been established, home uterine activity monitoring should not be used clinically. In the future, HUAM may play a cost-saving role in preventing preterm birth in specific high-risk subgroups, such as in multiple pregnancies, but this role needs to be tested before being specifically advocated.

Tocolytics: Drugs to Suppress Preterm Labor

The physiological trigger for labor both at term and preterm remains a mystery (see the article by Nathanielsz in this journal issue). At term, judging whether or not labor has started depends on the frequency of contractions and cervical dilation. Judging whether or not preterm labor has started is more difficult because contractions may occur without cervical dilation, and waiting for the cervix to dilate may lead to stronger contractions, which are more difficult to stop. Successful inhibition of preterm labor depends upon early diagnosis, but the diagnosis of preterm labor is erroneous up to 80% of the time.⁹ As a result, preterm labor is widely

overdiagnosed so as not to miss those minority of cases of true preterm labor. Over the years, a wide variety of drugs—called tocolytics—have been used in attempts to suppress preterm contractions. The effectiveness of several of these drugs is discussed below.

Betamimetics

Betamimetic agents are used more extensively than any other agents. All of these drugs are chemically and pharmacologically related to the catecholamines, compounds in the body that control involuntary muscles such as the heart and

The American College of Obstetricians and Gynecologists recommends that home uterine activity monitoring devices remain investigational and not be routinely used.

uterus. These drugs stimulate receptors in the uterus which cause the uterus to relax, thus stopping uterine contractions. Data on the effect of betamimetic drugs in controlled trials of preterm labor shows that they are successful in delaying delivery for up to two days. However, there is no associated decrease in the incidence of perinatal mortality or morbidity with the use of these drugs.^{10,11} One of the major benefits of using tocolytic drugs is to delay delivery long enough to give prenatal corticosteroids a chance to enhance the maturation of fetal lungs.¹¹ One may conclude that, conversely, little benefit may be reaped if glucocorticoids are not used.

Recent attention has been focused on a new way to administer the betamimetic drugs which uses a pump implanted under the skin to inject the drugs. The pump delivers small doses of the drug in short pulses, a method that is thought to maximize the effect of each small dose. Pregnancy was prolonged an average of nine weeks in a small group of women who failed oral betamimetic therapy, but used the pump.¹² Further studies are needed to validate this potentially promising approach.

Inhibitors of Prostaglandin Synthesis

There is substantial evidence that prostaglandins are of critical importance in the initiation and maintenance of human labor (see the article by Nathanielsz in this journal issue). Suppression of the body's

ability to produce prostaglandins is, therefore, a logical approach to the prevention of preterm labor. The most widely used inhibitor of prostaglandin synthesis in preterm labor is indomethacin. Two small studies found that the prostaglandin-inhibiting drugs may be effective in preventing preterm labor.^{13,14} Compared with betamimetic drugs, indomethacin is more effective in delaying delivery for up to two days. In addition, indomethacin delayed delivery slightly longer (7 to 10 days) than betamimetic drugs, and decreased the overall incidence of preterm delivery and low birth weight.^{15,16}

One of the major reasons prostaglandin inhibitors are not more widely used is that they are not innocuous drugs. In the mother, side effects such as stomach ulcers, gastrointestinal and other bleeding, and allergic reactions occur but are very rare. In the fetus, indomethacin has

that gained by glucocorticoid administration.

Calcium Antagonists

Over the past 10 years, calcium channel blockers have emerged as major agents for the control of preterm labor and for the treatment of hypertension in pregnancy. Because calcium is required to produce muscle contractions, agents that block the uptake of calcium in muscle cells will decrease the ability of the muscles to contract. In all studies, nifedipine, the most commonly used calcium blocker, has been as successful as betamimetics in delaying preterm labor.^{21,22} As with the betamimetics, magnesium sulfate, and indomethacin, there has been no real evidence for decreased perinatal morbidity and mortality with the use of calcium antagonists.

Combination Therapy

As all tocolytics have significant failure rates, especially in the face of advanced preterm labor, several groups have asked whether combination therapy may offer advantages. One randomized trial compared ritodrine alone with ritodrine and magnesium sulfate and found improved pregnancy prolongation with the combination therapy. Unfortunately, in two studies, one-half of the women receiving combination therapy developed severe side effects (cardiovascular symptoms or very fast heart rates).^{20,23} Most clinicians are reluctant to accept this high level of side effects given the small benefit that even single-agent therapy has shown. A combination that may have more benefit in the future is that of betamimetics and calcium channel blockers, which is currently under study.

Oxytocin Analogues

Recently, an oxytocin analogue which also blocks uterine contractility has been introduced.²⁴ Oxytocin is a compound that the body produces to stimulate uterine contractions. Oxytocin analogues may be used to prevent the action of oxytocin and thus prevent contractions. Further studies are needed to determine the efficacy of these promising drugs.

Summary

There is currently no evidence that the use of tocolytic drugs is effective in preventing preterm birth. Moreover, the use of these drugs is associated with many potentially severe side effects. There is strong evidence that tocolytic agents work to delay

One of the major benefits of using tocolytic drugs is to delay delivery long enough to give prenatal corticosteroids a chance to enhance the maturation of fetal lungs.

been associated with a severe interruption in the blood circulation between the baby's heart and lungs, and other serious side effects.

Magnesium Sulfate

Magnesium sulfate is a commonly used tocolytic, and in many institutions is the first-line therapy for preterm labor. The ability of magnesium to decrease uterine contractility has long been recognized, but the mechanism by which it does so is not known. In one trial, magnesium was found to have no significant effect on duration of gestation, birth weight, neonatal morbidity, and perinatal mortality.¹⁷ Compared with the other drugs, magnesium sulfate appears to be no better than other tocolytics.¹⁸⁻²⁰ The combination of ritodrine (a commonly used betamimetic drug) and magnesium sulfate resulted in a higher incidence of serious side effects with no greater benefit than ritodrine alone. There are no convincing data that magnesium sulfate delays delivery beyond two days, nor are there data to show a decrease in preterm delivery or an improvement in neonatal outcomes beyond

delivery for up to two days. This short delay is important as it can be used to allow time for corticosteroids to take effect and enhance fetal lung maturity, or to allow the mother to be transferred to a hospital with high-level neonatal intensive care facilities. The scientific evidence of efficacy available for all of these drugs is surprisingly scarce given the frequency of their use. There are few data to support using tocolytics without prenatal corticosteroid therapy to achieve a measurable decrease in perinatal morbidity and mortality.

Despite the availability of tocolytic agents and their extensive use, there has been no reduction in the overall incidence of low birth weight (less than 2,500 grams, or 5 pounds, 8 ounces) since the introduction of these drugs. In many instances of preterm labor, the use of tocolytic drugs is contraindicated, such as with uterine infections, bleeding, or severe maternal disease and, therefore, these drugs cannot be used. Thus, despite the short-term efficacy of tocolytic drugs, this technology has not made an impact on reducing overall low birth rate.²⁵

Corticosteroids: Drugs to Accelerate Fetal Lung Maturity

During the late 1960s, while studying the initiation of labor in sheep, it was observed that prematurely delivered lambs exposed prenatally to corticosteroids survived longer than placebo-treated control animals. A subsequent randomized, placebo-controlled trial of a corticosteroid, betamethasone, among pregnant women demonstrated clear reductions in the incidence of respiratory distress syndrome (lungs too immature to allow normal breathing) and neonatal mortality. A reduction in the incidence of respiratory distress syndrome was detected only if corticosteroids were given between one to seven days prior to the delivery.²⁶

Since this landmark study, other randomized trials have confirmed and extended these findings. In addition to the reduction of respiratory distress syndrome, studies have shown an overall reduction in neonatal death, cerebral hemorrhage (bleeding in the brain), and necrotizing enterocolitis (damage to the intestine). There was no strong evidence suggesting adverse effects of corticosteroids.²⁷ Infants who were exposed to cor-

ticosteroids before birth have been followed for three to six years and have shown no impairment in physical, cognitive, or psychosocial development.^{28,29}

Despite this overwhelming evidence that steroids are of great benefit in preventing morbidity and mortality in preterm infants, they are not universally used in all situations where they could be of benefit. It is estimated that only 12% to 18% of women who deliver very preterm

Antenatal steroid therapy could result in a substantial decrease in neonatal morbidity and mortality, and could produce substantial cost savings.

births are treated with antenatal corticosteroids.^{30,31} In contrast, tocolytic drugs are widely used, yet their benefit is not nearly so clear. The reason may be that the obstetrician sees the immediate benefit of tocolytic drugs in the cessation of contractions. However, the benefits of steroids are seen after the delivery and are, therefore, not as obvious to obstetricians. One need only look at the tremendous savings in dollars and time spent in the neonatal intensive care unit to see the clear benefits of antenatal steroid use.³¹

The conclusion of a recent consensus development conference sponsored by the National Institutes of Health is that antenatal steroid therapy is indicated for women at risk of preterm delivery and that its widespread use could result in a substantial decrease in neonatal morbidity and mortality, and could produce substantial cost savings. As a result of these conclusions, it behooves the obstetrician to look beyond the bedside and consider antenatal steroid administration when treating women with preterm labor because failure to do so is costly in terms of the health of the newborn and increased medical care costs.

Bed Rest to Prolong Pregnancy in Twin Pregnancies

Bed rest is a common recommendation for women whose pregnancies are complicated by one or more of a wide variety of conditions, such as multiple pregnancy,

preeclampsia (pregnancy-induced high blood pressure), spontaneous abortion, fetal growth retardation, and threatened preterm delivery. Despite little evidence of its effectiveness in preventing adverse outcomes, bed rest is used in nearly 20% of all pregnancies.³² Most notably, hospitalization for bed rest in twin pregnancies has been advised. Twin pregnancies account for approximately 1% of all pregnancies, but they account for approximately 10% of perinatal deaths.³³ Compared with singletons, the death rate among twins is considerably higher for every major cause of death.³³ Thus, in the belief that prolongation of pregnancy or some other improved outcome may result, bed rest, either in hospital or at home, has been commonly recommended by many clinicians, even in

It is not logical at present to prescribe routine bed rest or hospital admission for twin pregnancies.

the absence of preterm labor. Because hospitalization is a costly and socially disruptive procedure, a benefit in fetal or maternal outcome should be demonstrated before it is widely applied.^{34,35} Because scientific evidence on bed rest and singleton pregnancies is absent and because most of the research on bed rest and hospitalization has been conducted on women with twin pregnancies, an evaluation of those studies on the effectiveness of bed rest in improving twin pregnancy outcomes will be discussed.

Some small early studies appeared to show a decreased frequency of preterm birth and perinatal mortality with bed rest in the hospital in twin pregnancies.^{36–38} But none of the recent randomized controlled trials of bed rest in the hospital in twin pregnancies during the third trimester of pregnancy have shown a prolongation of pregnancy.^{39–41} However, results of the three trials suggest that there may be a decreased risk of developing hypertension and a reduced incidence of low birth weight from routine hospitalization. Initial studies of hospitalization in the second trimester of pregnancy (28 to 29 weeks of gestation) found no increase in the length of pregnancy.^{42,43}

In summary, it is not logical at present to prescribe routine bed rest or hospital

admission for twin pregnancies. Most of the studies have excluded women with complications such as bleeding during pregnancy, pregnancy-induced hypertension, polyhydramnios (increased amounts of amniotic fluid), and previous cervical cerclage or cesarean delivery. Thus, randomized controlled trials of bed rest in the hospital for complicated twin pregnancy or higher multiple pregnancy are needed before this treatment can be widely recommended.

In spite of the apparent simplicity of this treatment, bed rest has the potential to extract a large economic toll on families. Obviously, bed rest in the hospital is costly, but in most instances (75% of the time), physicians prescribe bed rest at home, which can also be extremely disruptive to the family. Prolonged bed rest may result in the loss of substantial income and employment, and may also result in serious side effects.³² In the absence of proof of the effectiveness of bed rest, its use should be curtailed sharply, and randomized trials should be conducted to see if bed rest at home or in the hospital actually does prevent the wide array of conditions for which it is currently used.

Delivery Methods for the Low Birth Weight Infant

Although many investigators have tried to determine the most effective way to deliver the low birth weight fetus, this issue remains controversial. Preterm infants have a higher incidence of brain hemorrhage, asphyxia, and birth trauma. Controversy persists about the merits of vaginal versus cesarean delivery to prevent these problems, especially if the fetus is in a breech presentation. Controversy also persists as to whether forceps should be used to protect the more fragile preterm fetal head. Additionally, it has long been thought that use of a generous episiotomy could reduce resistance and minimize the risk of injury to the preterm fetal head, although there are few data to support this theory.⁴⁴

Cesarean Delivery

Although some reports have shown that cesarean delivery of the low birth weight fetus may decrease trauma, most investigations do not show a fetal or neonatal advantage from cesarean delivery. The effect of delivery route on neonatal outcomes was studied in 17,260 mothers and failed to show any difference in the outcome

between infants in the vertex position (head down) who had delivered by cesarean or vaginally.⁴⁵ For all birth weight levels, there was no improvement in intrapartum or neonatal morbidity and mortality associated with the cesarean delivery. Cesarean birth should be reserved for those situations where there is fetal distress, with the same indications as at-term delivery. Thus, vaginal birth is the preferred route of delivery for the low birth weight infant in the normal vertex position.

It has long been recognized that a preterm infant with breech presentation carries an increased risk compared with the fetus in the vertex presentation at vaginal delivery. Vaginal delivery of breech preterm infants has been associated with the risk of entrapment of the head (the proportionally larger head of the preterm infant relative to its body gets stuck in the cervix after the body has already passed through), a greater likelihood of cord prolapse (This occurs when the umbilical cord slips past the body of the fetus and protrudes out the cervix. The cord is then compressed by the cervix, and the blood supply to the fetus is cut off.), and an increased risk for asphyxia.⁴⁶ No prospective trials of cesarean delivery versus vaginal delivery exist for the preterm breech infant, thus the only data come from non-randomized retrospective studies.

There are many problems with the validity of the results from retrospective studies. The main problem is deciding if the study results are due to the intervention or to the way the women were selected to undergo a cesarean or a vaginal delivery. It is likely that the women selected for cesarean delivery were those for whom more medical care may have been available or that their infants were felt to be healthy enough that the risk of vaginal breech delivery might not harm them. Conversely, fetuses who were thought to be already impaired may have been delivered by breech vaginal delivery to minimize morbidity to the mother with a fetus thought to be compromised. Furthermore, a number of the investigations were conducted over a long time period, during which our ability to care for the preterm neonate improved dramatically. Thus, an infant born in the early 1980s, regardless of the mode of delivery, would have a much greater risk of mortality than an infant born in the late 1980s because our

ability to care for preterm infants during this time period improved drastically.

Despite these limitations, general agreement is emerging that the outcome for very low birth weight (less than 1,500 grams, or 3 pounds, 5 ounces) infants in breech presentation is generally better after cesarean delivery than after vaginal delivery. Decreased rates of brain hemorrhage and decreased rates of neurologic handicaps have been demonstrated among very low birth weight infants who were delivered by cesarean.^{47,48} The ultimate answer to this question must come from prospective randomized studies. However, there is little chance that this type of study will be accomplished because of the widely held belief (based upon retrospective studies) that breech very low birth weight infants delivered by cesarean have improved outcomes. Thus, without formal testing, we will not know the optimal mode of delivery for all very low birth weight infants.

Episiotomy

An episiotomy, cutting of the mother's tissue between the vagina and the anus, is done during labor to create more space for the baby's head to descend. Its use has been suggested for the vaginal delivery of the low birth weight infant to reduce resistance and shorten the second stage of labor. The theoretical basis for this recommendation is to protect the soft fetal head from injury. However, the forces ap-

Without formal testing, we will not know the optimal mode of delivery for all very low birth weight infants.

plied by the perineum are much less than those generated by the cervix and muscles of the vagina through which the fetus has already passed. There are no data in the literature demonstrating that episiotomy improves neonatal outcomes.⁴⁹

Forceps

Forceps, metal tongs designed to grasp the fetal head, are used to help guide and remove the baby from the uterus. The use of forceps was initiated in the belief that it would protect the baby's head during delivery. In the 1960s, it was shown that low birth weight infants had better outcomes if they were delivered using forceps.⁵⁰ Re-

cent studies, however, have not shown a benefit from the use of forceps.⁴⁹ Moreover, it has been suggested that the use of forceps may even harm the fetus by increasing the incidence of brain hemorrhages.⁵¹ In spite of the lack of definitive evidence from clinical trials, routine use of forceps to protect the fetal head has been abandoned, and use of forceps in delivering the preterm fetus now has the same indications as for term deliveries.

Multifetal Pregnancy Reduction

Within the past decade, the American public has seen a rise in multifetal pregnancies as a result of widespread use of infertility therapies such as ovulation-inducing drugs, in vitro fertilization, gamete intrafallopian transfer, and zygote intrafallopian transfer. For example, in the United States in 1990, 5,193 babies were born with the aid of infertility therapies. Of those, 981 sets were twins, 158 sets were triplets, 12 were quadruplets, and 2 were quintuplets.⁵²

Unfortunately, the risks of perinatal mortality and morbidity and of maternal morbidity increase in multifetal pregnancies. The most common complication is preterm delivery, with twins having an average gestational age at delivery of 36 to

psychological and economic cost, and because future conceptions are not guaranteed, this option is usually the least desirable. Second, the couple can attempt to proceed with the pregnancy. Even though there are reports of survival of some or all of quadruplets and quintuplets, there is still significant risk of long-term morbidity. Survival with six or seven fetuses, although reported, is extremely rare, and there are no reports of any fetal survivals with eight or more fetuses. Finally, the couple can choose multifetal pregnancy reduction.

Over the past few years, multifetal pregnancy reduction has become a realistic option. Among the different techniques proposed for multifetal reduction, one approach, transabdominal potassium chloride, has been the most widely adopted. This involves an injection through the mother's abdomen into the most easily accessible fetus. The potassium chloride injection produces almost instantaneous death of the injected fetus. The fetal remains gradually degenerate and are often undetectable at delivery. This technique is usually performed at ten to twelve weeks of pregnancy, when the chance of spontaneous loss of the remaining embryos and the risk of complications from a retained nonviable fetus are less likely.⁵⁹

Several recent studies have evaluated the efficacy of transabdominal multifetal pregnancy reduction in improving outcomes.^{60–63} Improved outcomes were evident in twins reduced from quadruplets. No such benefit could be found for reduction of triplets to twins in terms of gestational age and mean birth weight, though triplets who were not reduced required a longer stay in the intensive care unit. Furthermore, twins resulting from multifetal reduction were born earlier and weighed less than twins who started out as twins. Thus, the clinical advantage of multifetal reduction for quadruplet pregnancies seems clear, but for triplet gestations, the procedure remains controversial. Twins who are reduced from higher order do not have outcomes as favorable as twins who start out as twins. It is not clear why this should be so; perhaps degenerative products from the retained nonviable fetus somehow cause preterm labor or preterm rupture of membranes. Recent evidence shows that reduced pregnancies have more complications such as placental abruption, preterm labor, and premature rupture of the membranes. The potential

There are no data in the literature demonstrating that episiotomy improves neonatal outcomes.

37 weeks; triplets, 34 weeks; quadruplets, 29 to 31 weeks, and quintuplets, even earlier.^{53–57} In addition, researchers have shown an increased incidence of low birth weight, gestational diabetes mellitus, pregnancy-induced hypertension, and greater requirement of neonates for hospital admission.^{53,56,57} Recent reports have shown that the outcomes with multifetal pregnancies have been improved by advances in prenatal care and intensive neonatal care.^{54,55}

A couple has several options when faced with a multifetal pregnancy.⁵⁸ First, they can electively terminate the multifetal pregnancy with the intent to conceive again. However, because the pregnancy is most likely wanted and achieved at great

for these complications should be discussed with mothers who wish to reduce triplets because the benefits of doing so are not clear.

Obviously, multifetal pregnancy reduction involves complex ethical issues. Abortion is safe, legal, and available to all women, and is not ethically different from multifetal reduction. If multifetal reduction improves the chances of survival of the remaining fetuses, many women may choose this option. Some women will be opposed to the procedure for the same reasons they would be opposed to an abortion, even if the outcomes for the remaining fetuses were improved. Therefore, individual choice will play a large part in making a decision for a reduction. This decision must be based not only on the possible medical benefits of the procedure, but also on the social and practical implications of raising multiple children simultaneously. In the future, with the advent of improved infertility technology, we should see a dramatic reduction in multiple births and, with it, a decreased need for multifetal pregnancy reduction.

Cervical Cerclage

The prevention of recurrent preterm delivery or pregnancy loss remains a challenge to modern obstetrics. It has been shown that the incidence of preterm delivery significantly increased with increasing numbers of previous second trimester losses from 3.7% if there were none to as high as 50% if there were two or more.⁶⁴ One important reason for recurrent pregnancy loss in the second trimester is incompetence of the uterine cervix (the inability of the cervix to maintain an intrauterine pregnancy until term). The incidence of this disorder has been reported to be between 0.5% and 1.3% in all pregnancies and between 16% and 20% among second trimester losses.⁶⁵ Despite many advances in modern obstetrics, much controversy remains regarding the diagnosis and treatment of cervical incompetence. The currently accepted treatment is cervical cerclage, or sewing closed the cervical opening. Cerclage appears to be effective when true cervical incompetence exists. Unfortunately, the diagnosis of cervical incompetence is very difficult and often inaccurate.

The causal mechanisms proposed for cervical incompetence include cervical trauma (trauma to the cervix during op-

erative or other procedures) and birth defects.⁶⁶⁻⁶⁸ Because the basic defect appears to be weakness of the internal opening of the cervix which leads to the uterus, surgical treatment has focused on closing the cervix at this level to allow the pregnancy to progress to term or at least until fetal viability (approximately 24 weeks of gestation). Placement of a cervical cerclage is associated with complications.⁶⁷

Despite many advances in modern obstetrics, much controversy remains regarding the diagnosis and treatment of cervical incompetence.

Rupture of the membranes, preterm contractions, and chorioamnionitis (uterine infection) may occur during or after the procedure. In addition, cervical dystocia (inability of the cervix to dilate normally in the course of labor) is seen more frequently after cerclage. Thus, one must consider these complications when deciding whether or not to perform a cerclage.

Attempts to evaluate the success rate of cervical cerclage in preventing recurrent pregnancy losses have been primarily retrospective. Furthermore, most studies have used women as their own control, that is, the results after cerclage are compared with the pregnancy outcomes of the same women before cerclage. This assumes that subsequent pregnancies have the same chance as prior pregnancies which may not necessarily be true. Nevertheless, studies have shown successful pregnancy outcome before cerclage as between 13% and 50% and after cerclage as between 71% and 89%.^{65,69-73}

A randomized trial of cervical cerclage found no evidence that it either prolonged gestation or improved survival.⁷⁴ In fact, women allocated to receive cerclage were hospitalized longer. However, the women eligible for this study may not have been at risk for cervical incompetence because many women at high risk for cervical incompetence were specifically excluded from the study, and many low-risk women may have been included in the study. A large multicenter randomized controlled trial showed that delivery tended to be later in the cerclage group. However, researchers estimated that, to prevent one very preterm delivery using cervical cer-

clage, they would need to use cerclage on 25 women. The results of this trial suggest that the operation of cervical cerclage could have an important beneficial effect in a minority of high-risk pregnant women.⁷⁵

One may conclude that a decision to do a cerclage must be on an individual basis, and it may greatly benefit a small number of women. However, there are some adverse effects of cerclage, and all trials are consistent in suggesting that cerclage increases obstetric interventions as judged by admission to hospital, the use of tocolytics, incidence of infection, induction of labor, and cesarean delivery. It seems that cerclage is effective when there is true cervical incompetence. However, the diagnosis of cervical incompetence during pregnancy is often difficult, and attempts to screen for this condition in nonpregnant women are unreliable. Thus, more efforts should be directed toward improved diagnosis of cervical incompetence.

For many years, investigators have searched for an objective method to detect cervical changes in the pregnant woman at risk for cervical incompetence. Ultrasound can be used in the lower uterine segment and cervical canal to help physicians visualize the cervical opening prior to delivery.⁷⁶ Recently, ultrasound viewing of the cervix through the vagina has appeared to provide more precise and de-

This ideal is rarely accomplished. We must carefully evaluate the scientific evidence on technology to prevent low birth weight and preterm birth in order to make policy decisions about which technologies should be encouraged and evaluated because of their potential to improve outcomes and which technologies should be discouraged because they do not make a difference.

Home uterine activity monitoring is an example of a system that was disseminated before it was shown to be effective. Most published studies have serious methodologic flaws, prompting the American College of Obstetricians and Gynecologists to advise that it remain investigational. This is not to say that HUAM has no role in obstetrics, but rather that further study is necessary to define that role. Perhaps HUAM will play an important and cost-saving role in the management of twins and triplets or other high-risk groups for preterm labor at home and actually save money in the long run. These are the types of issues which should have been addressed before this technology was released for general use without adequate data to define its role.

Tocolytics are an example of a technology which is so widely accepted and ingrained in medical practice that few clinicians question its usefulness. Many would be surprised to find that little benefit on a population basis has been found for these drugs beyond lengthening a pregnancy by about two days. With the combination of corticosteroids and tocolytics, great benefit has been found, yet corticosteroids are not nearly so widely utilized. This is beginning to change, as more clinicians become aware of the unequivocal benefit of steroids on neonatal outcomes. The reluctance on the part of many clinicians to use corticosteroids is somewhat baffling, but may be because obstetricians do not see the immediate benefit of steroids. It is hoped that the dissemination of the results of the recent Consensus Conference sponsored by the National Institutes of Health will stimulate the use of this life-saving technology.³⁰

Bed rest in the hospital to prevent preterm delivery is an example of an intervention which makes intuitive sense and is seemingly simple to carry out but is based upon little or no empirical evidence that it actually makes a difference. Given the exorbitant costs of a hospital stay and the social disruption that it causes, with little

It is essential that controlled trials be carried out for new techniques before they are widely distributed in the marketplace.

tailed information on cervical structure.⁷⁷ Ultrasound evaluation of the cervix offers an objective means of establishing the presence of cervical incompetence during pregnancy. Standardization of the scanning techniques and large prospective studies will be necessary to determine the value of this new diagnostic tool.

Conclusions

Obstetricians are very dependent on technology in their practice of medicine, and thus it is essential that controlled trials be carried out for new techniques before they are widely distributed in the marketplace.

effect on preventing preterm birth, there is no reason to prescribe prophylactic bed rest. However, many physicians continue to recommend bed rest for women at risk for preterm birth. Many interventions in medicine seem to make intuitive sense, and we must condition ourselves to continue to be scientific and test interventions before widely prescribing them simply because they seem to make sense.

Cesarean delivery for vertex, low birth weight infants is an example of a technology which was tested and found not to make a difference in outcome. Today, few institutions routinely perform cesarean deliveries on women who have a low birth weight infant in the vertex position. Likewise, episiotomy to protect the fetal head has become outmoded as the evidence mounted against its usefulness. The use of cesarean delivery for breech low birth weight infants is common practice, but it remains a controversial procedure. Randomized clinical trials are needed to test its efficacy before valid conclusions can be drawn.

Multifetal pregnancy reduction is a technology that is relevant for only a very small number of women and, as such, will not have a major impact on mortality. However, for individual parents, it may be vitally important. To a parent who does not believe in abortion, it may be a tremendous relief to know that reduction from triplets to twins will do little if anything to improve their neonates' outcomes. To a parent who cannot fathom the financial and emotional impact of bringing up four possibly impaired children, it may also be a tremendous relief to know that there is an intervention which is safe and effective in improving outcomes. Technology should be used not only to improve outcomes of multifetal pregnancies, but also to facilitate the lives of the parents taking care of the children created in this way. Ideally, in the future, reproductive technology will improve, and there will be a dramatic reduction in multiple births.

Cervical cerclage is an example of a technology that, despite being widely accepted, has never been tested in a truly randomized controlled trial. It is a technology with relatively minimal morbidity; therefore, the physicians of desperate couples who strongly desire children are often unwilling to take the chance that they will be assigned to the control group which does not receive the intervention. While

there does appear to be a benefit for those women with true cervical incompetence, it is very difficult to diagnose this condition accurately. Thus, many more women are diagnosed and unnecessarily treated with cerclage than truly have the disease. In fact, 25 women suspected to have cervical incompetence must undergo cerclage suturing to see a benefit in just one of those 25 women. Finding a way to diagnose true cervical incompetence will be the key to the successful use of this technology.

The reasons physicians use unproven technology or ignore proven ones is un-

There is no easy and effective way to modify physician behavior by encouraging the use of effective technologies such as corticosteroids and discouraging the use of ineffective or unproven technologies.

clear. At present there is no easy and effective way to modify physician behavior by encouraging the use of effective technologies such as corticosteroids and discouraging the use of ineffective or unproven technologies such as bed rest or home uterine monitoring. Limiting the availability of new technologies before they are proven to be effective is a first step. But it is difficult to remove familiar technologies despite their proven ineffectiveness. In the current climate of cost consciousness, it is imperative that the widespread use of these unproven and ineffective technologies be abandoned and that the use of proven technologies be encouraged. In addition, we must be careful *not* to use proven technology in those situations where it does not improve outcomes. Dissemination of technology into low-risk populations has the potential to do more harm than good. Finally, physicians need to be educated to be wise consumers of medical technologies. Up-to-date information, critical reviews, and a systematic synthesis of the thousands of trials that have evaluated obstetric technologies have been electronically compiled in the *Oxford Database of Perinatal Trials*⁷⁸ and published in *Effective Care in Pregnancy and Childbirth*⁷⁹ and *A Guide to Effective Care in Pregnancy and Childbirth*.⁸⁰ These important resources provide physicians with unbiased, clear recommenda-

tions about which technologies are effective and warn against using those that are not.

The use of obstetrical technologies appears to have had little impact on reducing the occurrence of low birth weight or preterm births.

The use of obstetrical technologies appears to have had little impact on reducing the occurrence of low birth weight or preterm births. Nationally, rates of low birth weight and preterm birth have not

changed appreciably in the past 25 years despite the introduction of many obstetrical technologies, procedures, and drugs. The reason for this apparent contradiction is that many of the currently used technologies are not effective. There is no effective way to stop the progress of labor once it has started, and attempts to devise an early detection system have generally been unsuccessful. One major handicap in developing methods to stop the progression of labor is that the mechanisms that produce preterm labor are not well understood. Much more work is needed to discover just how and why labor is initiated before new preventive technologies can be developed.

1. Sachs, B., Hellerstein, S., Freeman, R., et al. Home monitoring of uterine activity: Does it prevent prematurity? *New England Journal of Medicine* (1991) 325:1374–77.
2. American College of Obstetrics and Gynecology. Home uterine activity monitoring. *Maternal and Fetal Medicine* (September 1992) 115:1–3.
3. Morrison, J., Martin, J., Martin, R., et al. Prevention of preterm birth by ambulatory assessment of uterine activity: A randomized study. *American Journal of Obstetrics and Gynecology* (1987) 156:536–43.
4. Hill, W., Fleming, A., Martin, R., et al. Home uterine activity monitoring is associated with a reduction in preterm birth. *Obstetrics and Gynecology* (1990) 76:13S–18S.
5. Iams, J., Johnson, F., and O'Shaughnessy, R. A prospective randomized trial of home uterine activity monitoring in pregnancies at increased risk of preterm labor. *American Journal of Obstetrics and Gynecology* (1988) 159:595–603.
6. Scioscia, A., Nickless, N., Hodgson, P., et. al. A randomized clinical trial of outpatient monitoring of uterine contractions in women at risk for preterm delivery: Self-palpation versus tocodynamometer. Paper presented at the Eighth Annual Meeting of the Society of Perinatal Obstetricians. Las Vegas, NV. 1988.
7. Mou, S., Sunderji, S., Gall, S., et al. Multicenter randomized clinical trial of home uterine activity monitoring for detection of preterm labor. *American Journal of Obstetrics and Gynecology* (1991) 165:858–66.
8. Grimes, D., and Schulz, K. Randomized controlled trials of home uterine activity monitoring: A review and critique. *Obstetrics and Gynecology* (1992) 79:137–42.
9. O'Driscoll, M. Discussion. In *Preterm labour*. A. Anderson, R. Beard, J.M. Brudenell, and P.M. Dunn, eds. Proceedings of the Fifth Study Group of the Royal College of Obstetricians and Gynaecologists. London: Royal College of Obstetricians and Gynaecologists, 1977, pp. 369–70.
10. Chalmers, I., Enkin, M., and Keirse, M., eds. *Effective care in pregnancy and childbirth*. Vol. 1. Oxford: Oxford University Press, 1989, pp. 715–21.
11. The Canadian Preterm Labor Investigators Group. Treatment of preterm labor with the beta-adrenergic agonist ritodrine. *New England Journal of Medicine* (1992) 327:308–12.
12. Lam, F., Gill, P., Smith, M., et al. Use of the subcutaneous terbutaline pump for long-term tocolysis. *Obstetrics and Gynecology* (1988) 72:810–13.
13. Niebyl, J., Blake, D., White, R., et al. The inhibition of preterm labor with indomethacin. *American Journal of Obstetrics and Gynecology* (1980) 136:1014–19.

14. Zuckerman, H., Reiss, U., and Rubinstein, I. Inhibition of human preterm labor by indomethacin. *Obstetrics and Gynecology* (1974) 44:787–92.
15. Katz, Z., Lancet, M., Yemini, M., et al. Treatment of premature labor contractions with combined ritodrine and indomethacin. *International Journal of Gynaecology and Obstetrics* (1983) 21:337–42.
16. Gamissans, O., Canas, E., Cararach, V., et al. A study of indomethacin combined with ritodrine in threatened preterm labor. *European Journal of Obstetrics, Gynecology, and Reproductive Biology* (1978) 8:123–28.
17. Cox, S., Sherman, M., and Leveno, K. Randomized investigation of magnesium sulfate for prevention of preterm birth. *American Journal of Obstetrics and Gynecology* (1990) 163:767–72.
18. Cotton, D., Strassner, H., Hill, L., et al. Comparison of magnesium sulfate, terbutaline, and placebo for inhibition of preterm labor: A randomized study. *Journal of Reproductive Medicine* (1984) 29:92–97.
19. Tchilinguirian, N., Najem, R., Sullivan, G., et al. The use of ritodrine and magnesium sulfate in the arrest of premature labor. *International Journal of Gynaecology and Obstetrics* (1984) 22:117–23.
20. Ferguson, J., Hensleigh, P., and Kredenster, D. Adjunctive use of magnesium sulfate with ritodrine for preterm labor tocolysis. *American Journal of Obstetrics and Gynecology* (1984) 148:166–71.
21. Read, M., and Wellby, D. The use of a calcium antagonist (nifedipine) to suppress preterm labor. *British Journal of Obstetrics and Gynaecology* (1986) 93:933–37.
22. Ferguson, J., Dyson, D., Schutz, T., et al. A comparison of tocolysis with nifedipine or ritodrine: Analysis of efficacy and maternal, fetal and neonatal outcome. *American Journal of Obstetrics and Gynecology* (1990) 163:105–11.
23. Hatjis, C., Swain, M., and Nelson, L. Efficacy of combined administration of magnesium sulfate and ritodrine in the treatment of premature labor. *Obstetrics and Gynecology* (1987) 69:317–22.
24. Melin, P., Trojnar, J., Johansson, B., et al. A synthetic antagonist of the myometrial response to oxytocin and vasopressin. *Journal of Endocrinology* (1986) 111:125–31.
25. Tejani, N., and Verma, U. Effect of tocolysis on incidence of low birth weight. *Obstetrics and Gynecology* (1983) 61:556–58.
26. Liggins, G., and Howie, R. A controlled trial of antepartum glucocorticoid treatment for prevention of the respiratory distress syndrome in premature infants. *Pediatrics* (1972) 50:515–25.
27. Crowley, P., Chalmers, I., and Keirse, M. The effects of corticosteroid administration before preterm delivery: An overview of the evidence from the controlled trials. *British Journal of Obstetrics and Gynaecology* (1990) 97:11–25.
28. MacArthur, B., Howie, R., Dezoete, J., et al. School progress and cognitive development of 6-year-old children whose mothers were treated antenatally with betamethasone. *Pediatrics* (1982) 70:99–105.
29. Collaborative Group on Antenatal Steroid Therapy. Effects of antenatal dexamethasone administration in the infant: Long-term follow-up. *Journal of Pediatrics* (1984) 104:259–63.
30. National Institutes of Health. *NIH Consensus Development Conference on Effect of Corticosteroids for Fetal Maturation on Perinatal Outcomes: February 28–March 2, 1994*. Bethesda, MD: U.S. Department of Health and Human Services, 1994.
31. Avery, M. The argument for prenatal administration of dexamethasone to prevent respiratory distress syndrome. *Journal of Pediatrics* (1984) 104:240.
32. Goldenberg, R.L., Cliver, S.P., and Bronstein, J. Bed rest in pregnancy. *Obstetrics and Gynecology* (1994) 84:131–36.
33. Botting, B., Davies, I., and MacFarlane, A. Recent trends in the incidence of multiple births and associated mortality. *Archives of Disease in Childhood* (1987) 62:941–50.

34. Powers, W., and Miller, T. Bed rest in twin pregnancy: Identification of a critical period and its cost implications. *American Journal of Obstetrics and Gynecology* (1979) 134:23–29.
35. Maloni, J., Chance, B., Zhang, C., et al. Physical and psychosocial side effects of antepartum hospital bed rest. *Nursing Research* (1993) 42:197–203.
36. Komaromy, B., and Lampe, L. The value of bed rest in twin pregnancies. *International Journal of Gynaecology and Obstetrics* (1977) 15:262–66.
37. Kappel, B., Hansen, K., Moller, J., et al. Bed rest in twin pregnancy. *Acta Geneticae Medicae et Gemellologiae* (1985) 34:67–71.
38. Gilstrap, L., Hauth, J., Hankins, G., et al. Twins: Prophylactic hospitalization and ward rest at early gestational age. *Obstetrics and Gynecology* (1987) 69:578–81.
39. Hartikainen-Sorri, A., and Jouppila, P. Is routine hospitalization needed in antenatal care of twin pregnancies? *Journal of Perinatal Medicine* (1984) 12:31–34.
40. Saunders, M., Dick, J., Brown, I., et al. The effects of hospital admission for bed rest on the duration of twin pregnancy: A randomised trial. *Lancet* (1985) 2:793–95.
41. Crowther, C., Neilson, J., Verkuyl, D., et al. Preterm labour in twin pregnancies: Can it be prevented by hospital admission? *British Journal of Obstetrics and Gynaecology* (1989) 96:850–53.
42. Crowther, C., Verkuyl, D., Neilson, J., et al. The effects of hospitalization for rest on fetal growth, neonatal morbidity and length of gestation in twin pregnancy. *British Journal of Obstetrics and Gynaecology* (1990) 97:872–77.
43. MacLennan, A., Green, R., O'Shea, R., et al. Routine hospital admission in twin pregnancy between 26 and 30 weeks' gestation. *Lancet* (1990) 335:267–69.
44. Ock Ahn, M., Yul Cha, K., and Phelan, J. The low birth weight infant: Is there a preferred route of delivery? *Clinics in Perinatology* (1992) 19:411–23.
45. Rosen, M., and Chik, L. The association between cesarean birth and outcome in vertex presentation: Relative importance of birth weight, Dubowitz scores, and delivery route. *American Journal of Obstetrics and Gynecology* (1984) 150:775–79.
46. Westgren, M., and Paul, R. Delivery of the low birth weight infant by cesarean section. *Clinical Obstetrics and Gynecology* (1985) 28:752–62.
47. Lamont, R., Dunlop, P., Crowley, P., et al. Spontaneous preterm labour and delivery at under 34 weeks gestation. *British Medical Journal* (1983) 286:454–57.
48. Effer, S., Saigal, S., Rand, C., et al. Effects of delivery method on outcome in the very low birth weight breech infant: Is the improved survival related to cesarean section or other perinatal care maneuvers? *American Journal of Obstetrics and Gynecology* (1983) 145:123–28.
49. Barrett, J., Boehm, F., and Vaughn, W. The effect of type delivery on neonatal outcome in singleton infants of birth weight of 1,000 grams or less. *Journal of the American Medical Association* (1983) 250:625–29.
50. Bishop, E., Israel, S., and Briscoe, C. Obstetric influences on the premature infant's first year of development: A report from the Collaborative Study of Cerebral Palsy. *Obstetrics and Gynecology* (1965) 26:628–35.
51. O'Driscoll, K., Meagher, D., MacDonald, D., et al. Traumatic intracranial hemorrhage in firstborn infants and delivery with obstetric forceps. *British Journal of Obstetrics and Gynaecology* (1981) 88:577–81.
52. Petrikovsky, B., and Vintzileos, A. Management and outcome of multiple pregnancy of high fetal order: Literature review. *Obstetrical and Gynecological Survey* (1989) 44:578–84.
53. Sassoon, D., Castro, L., Davis, J., et al. Perinatal outcome in triplet versus twin gestations. *Obstetrics and Gynecology* (1990) 75:817–20.
54. Newman, R., Hamer, C., and Miller, M. Outpatient triplet management: A contemporary review. *American Journal of Obstetrics and Gynecology* (1989) 161:547–55.
55. Collins, M., and Bleyl, J. Seventy-one quadruplet pregnancies: Management and outcome. *American Journal of Obstetrics and Gynecology* (1990) 162:1384–92.

56. Seoud, M., Toner, J., Kruithoff, C., et al. Outcome of twin, triplet, and quadruplet in vitro fertilization pregnancies: The Norfolk experience. *Fertility and Sterility* (1992) 57:825–34.
57. Rebar, R., Luke, B., and Keith, L. The contributions of singletons, twins and triplets to low birth weight, infant mortality and handicap in the United States. *Journal of Reproductive Medicine* (1992) 37:661–66.
58. Evans, M., Littmann, L., King, M., et al. Multiple gestation: The role of multifetal pregnancy reduction and selective termination. *Clinics in Perinatology* (1992) 19:345–57.
59. Frederiksen, M., Keith, L., and Sabbagha, R. Fetal reduction: Is this the appropriate answer to multiple gestation? *International Journal of Fertility* (1992) 37:8–14.
60. Melgar, C., Rosenfeld, D., Rawlinson, K., et al. Perinatal outcome after multifetal reduction to twins compared with nonreduced multiple gestations. *Obstetrics and Gynecology* (1991) 78:763–67.
61. Porreco, R., Burke, S., and Hendrix, M. Multifetal reduction of triplets and pregnancy outcome. *Obstetrics and Gynecology* (1991) 78:335–38.
62. Berkowitz, R., Lynch, L., Lapinski, R., et al. First-trimester transabdominal multifetal pregnancy reduction: A report of two hundred completed cases. *American Journal of Obstetrics and Gynecology* (1993) 169:17–21.
63. Evans, M., Dommergues, M., Wapner, R., et al. Efficacy of transabdominal multifetal pregnancy reduction: Collaborative experience among the world's largest centers. *Obstetrics and Gynecology* (1993) 82:61–66.
64. Keirse, M., Rush, R., Anderson, A., et al. Risk of pre-term delivery in patients with previous pre-term delivery and/or abortion. *British Journal of Obstetrics and Gynaecology* (1978) 85:81–85.
65. Kuhn, R., and Pepperell, R. Cervical ligation: A review of 242 pregnancies. *Australian and New Zealand Journal of Obstetrics and Gynaecology* (1977) 17:7083.
66. Ludmir, J. Managing the incompetent cervix. *The Female Patient: Practical Ob/Gyn Medicine* (1988) 13,7:63–68.
67. Golan, A., Barnan, R., Wexler, S., et al. Incompetence of the uterine cervix. *Obstetrical and Gynecological Survey* (1989) 44:96–107.
68. Jewelewicz, R. Incompetent cervix: Pathogenesis, diagnosis and treatment. *Seminars in Perinatology* (1991) 15:156–61.
69. Harger, J. Comparison of success and morbidity in cervical cerclage procedures. *Obstetrics and Gynecology* (1980) 56:543–48.
70. Jennings, C. Temporary submucosal cerclage for cervical incompetence: Report of forty-eight cases. *American Journal of Obstetrics and Gynecology* (1972) 113:1097–1102.
71. McDonald, I. Cervical cerclage. *Clinics in Obstetrics and Gynaecology* (1980) 7:461–79.
72. Crombleholme, W., Minkoff, H., Delke, I., et al. Cervical cerclage: An aggressive approach to threatened or recurrent pregnancy wastage. *American Journal of Obstetrics and Gynecology* (1983) 146:168–74.
73. Novy, M., Haymond, J., and Nichols, M. Shirodkar cerclage in a multifactorial approach to the patient with advanced cervical changes. *American Journal of Obstetrics and Gynecology* (1990) 162:1412–20.
74. Rush, R., Isaacs, S., McPherson, K., et al. A randomized controlled trial of cervical cerclage in women at high risk of spontaneous preterm delivery. *British Journal of Obstetrics and Gynaecology* (1984) 91:724–30.
75. MRC/RCOG Working Party on Cervical Cerclage. Final report of the Medical Research Council/Royal College of Obstetricians and Gynaecologists multicentre randomized trial of cervical cerclage. *British Journal of Obstetrics and Gynaecology* (1993) 100:516–23.
76. Sarti, D., Sample, W., Hobel, C., et al. Ultrasonic visualization of a dilated cervix during pregnancy. *Radiology* (1979) 130:417–20.

77. Andersen, F., Nugent, C., Wanty, S., et al. Prediction of risk for preterm delivery by ultrasonographic measurement of cervical length. *American Journal of Obstetrics and Gynecology* (1990) 163:859–67.
78. Chalmers, I. *Oxford database of perinatal trials*. Version 1.2, Spring 1992 disk issue 7. Oxford: Oxford University Press, 1992.
79. See note no. 10, Chalmers, Enkin, and Keirse, for a discussion of effective care during pregnancy and childbirth.
80. Enkin, M., Keirse, M., and Chalmers, I. *A guide to effective care in pregnancy and childbirth*. Oxford: Oxford University Press, 1989.

The Role of Social Change in Preventing Low Birth Weight

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Abstract

The authors of this article examine the relationship between social factors and low birth weight and the ways in which disparities in socioeconomic status have been addressed over time. The evidence regarding the effectiveness of various efforts to influence birth weight by mitigating the consequences of disadvantage are also assessed. Low socioeconomic status has been shown to influence low birth weight through its various correlates. Historically and today, most programs and policies directed at low birth weight prevention attempt to address the individual health consequences of economic and social disadvantage. By and large, these efforts have produced mixed results. Efforts to affect low birth weight by addressing the underlying causes of social and economic disadvantage have been similarly inconclusive, reflecting the paucity of research on the subject, as well as the historical and ongoing failure to make the research link between health and social policy. The authors argue that reducing persistent disparities in low birth weight requires several steps, including embracing a broader definition of health which incorporates social dimensions, recasting the focus of research and interventions from pregnancy outcomes and infant health exclusively to include the notion of women's health more globally, expanding the research agenda to unravel the paradox of socioeconomic factors and health, and pursuing a dedicated, national commitment to assuring adequate support to individuals and families, including both adequate income and health care.

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Social factors define a range of social, cultural, and economic circumstances that are shared by people with similar levels of financial and educational resources. They are often defined by a single factor that describes an individual, such as income, occupation, or educational level. More broadly, they are defined as one's neighborhood income level, neighborhood crime level, or a composite of individual and area factors. The complex relationship of social factors has proved very difficult to measure accurately, and few national data sources include information about both social factors and health characteristics.¹

Social factors and disease are undeniably linked.²⁻⁶ Women who live in poverty, who have low levels of education, who work in low-wage jobs, and who have few other social resources are more likely to suffer adverse birth outcomes than are more advantaged women.⁷⁻¹³ Yet social programs designed to improve the health of women and children in the United States have had mixed results. Today, most

programs and policies directed at preventing low birth weight attempt to address the health consequences of economic and social disadvantage rather than its underlying causes. This lack of integration of social strategies with health has been a major barrier to reducing the high rates of low birth weight in the United States.

In this article, we analyze the relationship between social factors and low birth weight in the United States, and examine some of the social strategies designed to improve the health of women and chil-

Socioeconomic status is one of the most powerful risk factors for poor health outcomes.

dren. We summarize the existing information describing the relationship between social factors and low birth weight, examine the history of social programs designed to improve the health status of women and children, and summarize the effectiveness of public policies enacted to improve the health of infants. Finally, we offer recommendations relating to both the research and policy arenas which may be used to improve the social and economic circumstances of women in the United States, thereby reducing rates of low birth weight and preterm birth.

The Health-Related Effects of Socioeconomic Status

Socioeconomic status is one of the most powerful risk factors for poor health outcomes. Persons of lower socioeconomic status suffer disproportionately from nearly all diseases and have higher rates of mortality than people of higher socioeconomic status.²⁻⁶ Recognition of this association is neither new nor limited to select causes of death or health problems. Observers noted as early as the Middle Ages that wealth and poverty influenced the distribution of disease.¹⁴ Among the conditions for which strong associations with socioeconomic status have been established are overall mortality,^{1,5,15,16} cardiovascular diseases and outcomes,^{17,18} infant and maternal mortality,¹⁹ unintended injury, homicide and suicide,¹⁹ and the prevalence of various diseases, including arthritis, heart disease, ulcers, diabetes,

hypertension, and chronic bronchitis.^{19,20} These associations persist both at the aggregate or area level and at the individual level.²¹

Low Birth Weight

Like many other health conditions, low birth weight is strongly associated with socioeconomic status. Studies in this country and others show that rates of low birth weight increase with decreasing socioeconomic status.^{7-13,22} This association persists across various measures of socioeconomic status, including occupation of the mother and/or father,^{23,24} income,^{25,26} and education.²⁷⁻²⁹ At the individual level, a major study conducted in Great Britain found the risk of preterm delivery to be 50% higher³⁰ and the risk of a term low birth weight delivery to be 95% higher³¹ among women in lower social classes. In the United States, women on lower socioeconomic levels have been found to be at significantly higher risk of preterm delivery, even when controlling for other known risk factors such as prepregnant weight, weight gain, alcohol and tobacco consumption, race, parity, and source of prenatal care.¹¹ At the geographic level, some but not all studies³² have found that, for any defined area, the more socioeconomically disadvantaged the population, the higher the incidence of low birth weight.^{25,33,34}

It is not clear just how low socioeconomic status actually causes an increased risk for low birth weight. It is thought that poverty—which is associated with reduced access to health care, poor nutrition, lower education, and inadequate housing—may be responsible for some of the increased risk.^{26,35-37} Low socioeconomic status is also strongly linked to other factors such as individual behavior, and race and ethnicity. Each of these factors has also been shown to be associated with higher rates of low birth weight. We examine the influence of these factors below and try to clarify their relationships with low socioeconomic status and birth outcomes.

Individual Behaviors

It is clear that individual behavior is closely linked to the social and economic culture in which one lives and that behaviors which affect one's health may act as a mediating pathway between social class and adverse health outcomes. It is often difficult to separate the effects of individual behavior and social class in relation to low birth weight. One individual behavior

that is highly correlated with socioeconomic status is cigarette smoking.^{38,39} Smoking is, in turn, more common among women in lower income groups than it is among women from higher income groups.¹⁹ Thus, the association between smoking and low birth weight can be viewed as arising from two sources—being from a low socioeconomic group or having an adverse lifestyle.

Rush and Cassano studied the relationship between socioeconomic status (measured by occupational grade) and low birth weight in more than 150,000 births occurring in Britain during 1970 and demonstrated that socioeconomic status and cigarette smoking had important but independent effects on low birth weight.⁴⁰

Whether health behaviors other than cigarette smoking account for higher rates of low birth weight among disadvantaged women is uncertain. (See the article by Chomitz, Cheung, and Lieberman in this journal issue.) Chronic, heavy alcohol drinking, while associated with low birth weight,⁴¹ is less common among women who live in poverty, and more common among women at higher income levels. Pregnant women who are insured by Medicaid are less likely to drink alcohol than their non-Medicaid-covered counterparts.⁴¹

With respect to illicit drug use during pregnancy, it is unclear whether poor women are more likely than nonpoor women to abuse illegal substances during pregnancy. Reports of increased use of illegal drugs during pregnancy by poor women may be attributed to the types of drugs that are studied and to the sites under study.^{42–44}

While individual behaviors can influence birth outcome, they do not fully explain the socioeconomic effect. However, it may also be possible that, while the use of alcohol or illegal drugs is lower among low-income women, the impact and consequences of these adverse lifestyle choices are exacerbated by poverty.³⁷ Researchers have noted that comparable stressful events have stronger negative effects on individuals of lower socioeconomic status than on those of higher socioeconomic status. Thus, different social class groups may have differing vulnerabilities to the same behavior.⁴⁵

Race/Ethnicity

The extent to which race and ethnicity explain the relationship between socioeconomic status and low birth weight is uncertain. Clearly, race as the primary explanation for the association between socioeconomic status and low birth weight has not been demonstrated. An association is often suggested, however, because the incidence of low birth weight is especially high among certain racial and ethnic minorities, especially African Americans.⁴⁶

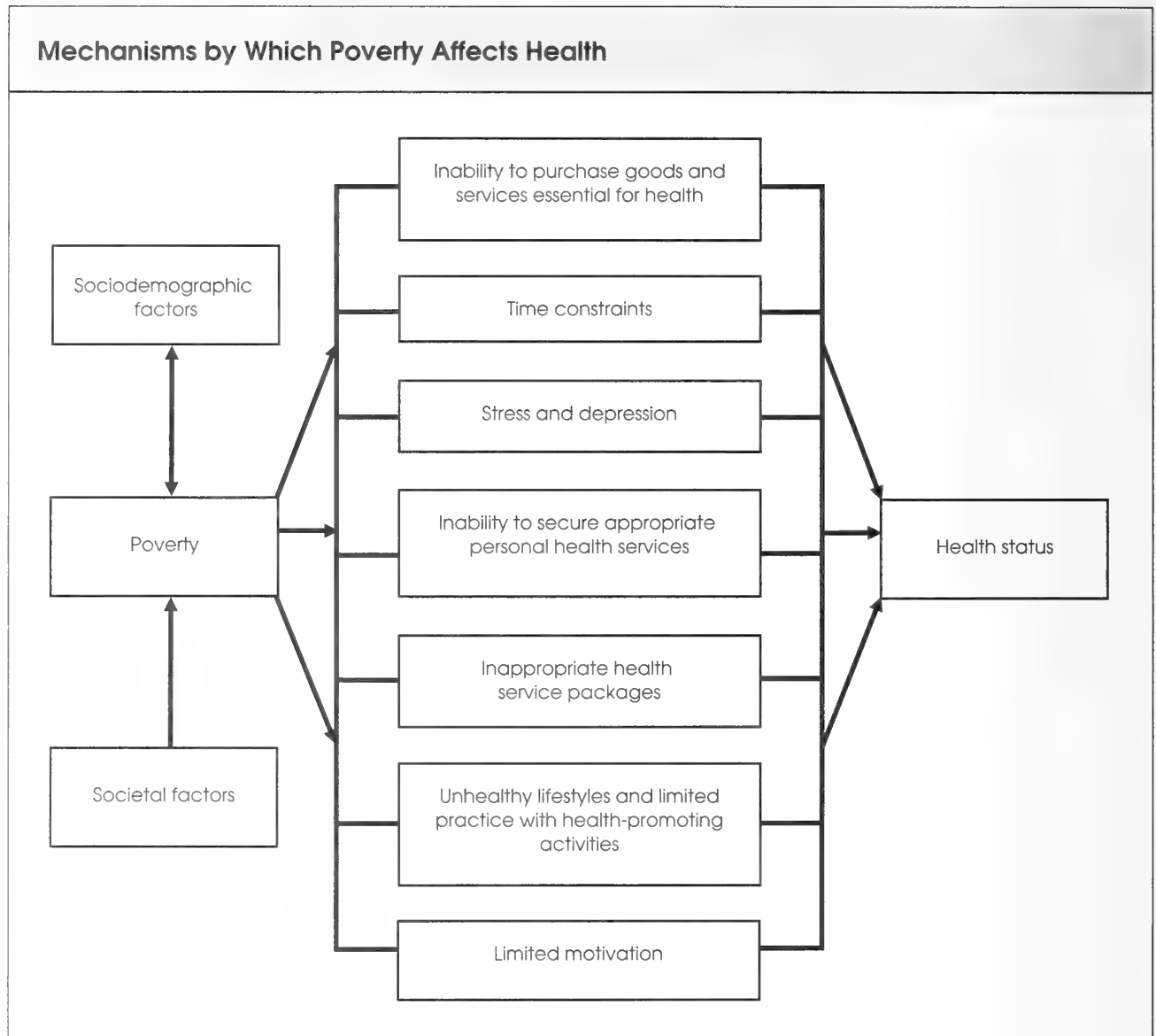
The extent to which race and ethnicity explain the relationship between socioeconomic status and low birth weight is uncertain.

In addition, persons in racial and ethnic minorities are significantly more likely to be poor, to have limited education, to live in substandard housing, and to be unemployed than their white counterparts.⁴⁷

Yet, while the relationship between race/ethnicity and socioeconomic status is strong, it does not demonstrate necessarily that the association between socioeconomic status and low birth weight is attributable to the high proportion of minorities in the lower socioeconomic strata. Studies that examine differences in rates of low birth weight by race produce mixed results when taking income into account. While a minority of studies have concluded that socioeconomic status explains the racial disparities in low birth weight,^{25,33} the majority of studies have found that the racial disparities in low birth weight are not due to socioeconomic status and that race and socioeconomic status have separate, independent effects on low birth weight rates.^{48–50}

Other reports have found little difference in the low birth weight distribution among black infants by income⁵¹ and wider differences in low birth weight rates between black and white infants at the upper end of the socioeconomic spectrum.⁴⁸ The finding of persistently high rates of low birth weight among African Americans may be explained by generations of poverty,²⁵ a higher concentration of black infants at the near-poor income level,⁴⁹ racism,⁵² or a combination of these

Figure 1



Source: Klerman, L. *Alive and well? A research and policy review of health programs for poor young children*. New York: National Center for Children in Poverty, Columbia University, 1991.

factors. However, research documenting these associations is lacking.

Access to Health Care Services

Limited access to basic health care services may also help to explain the socioeconomic differences in health.^{2,21,53,54} While higher rates of mortality occur in lower socioeconomic groups in general, not all individuals in low socioeconomic groups have higher risks for mortality. Kaplan and colleagues² explain this paradox in terms of demands and resources. Persons of lower socioeconomic status face greater social and community demands while having fewer resources (including money, access to medical care, interper-

sonal resources such as social supports, and personal resources such as coping mechanisms). The extent and pressure of these two forces is variable for individuals, thus explaining variation in health status within low socioeconomic groups.

In a summary of the research on health programs for poor young children, Klerman³⁷ proposed a framework for examining how poverty affects pregnancy which complements the work by Kaplan. In the Klerman model, sociodemographic factors, societal forces (including discrimination), and poverty interact to produce a number of circumstances that negatively influence health status (see Figure 1). Put

another way, because women within low socioeconomic groups face varying degrees of demands and have different levels of resources with which to mediate those demands, the health status of persons within these groups is likely to vary as well.

Health and Social Policy in the United States

Given the association between socioeconomic status and low birth weight, what effect have social policies had on mitigating this relationship? Many excellent histories have been written about this country's investments in mothers and children.^{55–58} The purpose of this section is to focus primarily on those points in history when opportunities to address directly the socioeconomic determinants of poor birth outcomes appeared to be present, either because of an interest in improving pregnancy outcome or because of an interest in addressing issues related to poverty.

Social Reform and the Progressive Era

America first confronted infant mortality as a social problem in the late nineteenth century, when many of the same issues that are at the center of the health care reform debate today were raised. These issues include the relationship of infant mortality to poverty, race, and ethnicity; the extent to which infant mortality is a behavioral as well as a socioeconomic problem; and the scope of government responsibility to combat it.⁵⁵ Prior to the creation of the Children's Bureau in 1912, the federal government accepted no formal responsibility for the health of mothers and children or for assuring adequate income and basic resources.⁵⁹ This changed, in part, as a result of the social reform movements of the period, which combined service provision with social reform.⁶⁰ More important, these social efforts gave way to a transformation in society's views of children. Initially, children were perceived largely in utilitarian terms, particularly among the working class, who had to rely on them to contribute to family earnings and to perform domestic duties. It was not until the early 1900s that childhood came to be viewed as a time of growth and development during which proper nurture was essential.^{56,61} With this change came a push toward, and an acceptance of, a greater role of the federal government in the promotion of the health of infants and

children through the federal Children's Bureau.⁶²

In its early years, the Children's Bureau addressed infant and child health as one issue in a continuum of social and economic needs.⁶³ A report issued by the bureau in 1916 highlighted the contribution of low paternal income to poor birth outcomes. However, these findings appear to have had little influence on federal poli-

The Sheppard Towner Act in 1929 was the primary federal strategy to improve birth outcomes.

cies and programs designed to improve pregnancy outcomes, which emphasized personal behavior and ignorance as the primary contributors to poor health.⁵⁵ With the enactment of the Sheppard Towner Act in 1929, the primary federal strategy to improve birth outcomes was the provision of direct services to individuals, notably educational and preventive health services, which built on the experience gained with the establishment of milk stations earlier in the century.⁵⁵ Under this act, public health nurses became the backbone of a program of permanent administrative units at the federal and state levels which oversaw and provided a range of services to expectant mothers, including education, breast-feeding support, milk stations, and prenatal health supervision.⁵⁶

The Great Depression

Thinking about social needs was revolutionized by the Great Depression as policymakers and the public became convinced that reliance on the private market alone was insufficient to assure economic security.⁶⁴ The most significant piece of social welfare legislation from this period was the Social Security Act, which established in 1935 a federal role in social welfare and income security.

Despite the significance of the Social Security Act, the law fell short of making the link between health outcomes and low socioeconomic status. Passage of the act resulted from a political compromise that eliminated provisions for a minimum level of family subsistence and any proposals for comprehensive national health insurance.⁶⁵ In addition, this act instituted a

dual system for federally supported income maintenance which assigned poor children (and therefore, their mothers) to a largely unpopular and financially precarious assistance program.⁶⁴ Adults with a record of work effort benefitted from a

The most important social legislation in this country's history fell short of assuring that all poor women of childbearing age would be protected from poverty.

federally administered income insurance program that was strongly supported politically. In contrast, the federally aided but state-administered assistance programs for selected groups, including the Aid for Dependent Children (ADC) program, reflected the persisting ambivalence about all non-work-related relief.⁶⁴ Thus, the most important social legislation in this country's history fell short of assuring that all poor women of childbearing age would be protected from the consequences of poverty.

"Poverty Amidst Plenty"

The 1960s and 1970s

By the 1960s, reports of "poverty amidst plenty" mounted, leading to a redirection of national attention toward ensuring better equity and addressing the needs of the underserved. This resulted in the creation of extensive social and health programs, including neighborhood health centers, the maternal and infant care projects, and the creation of Medicare and Medicaid.⁶⁶

The enactment of Medicare and Medicaid, both passed in 1965, mirrored the two-tiered approach of the Social Security Act. Medicare was enacted as federally administered insurance covering all elderly persons regardless of income, while Medicaid—the primary source of health insurance for poor women of reproductive age—was enacted as a means-tested, state-based program with vast variability in eligibility and scope of services.⁶⁷

Despite these limitations, impressive gains were achieved during this period. An expanding economy helped to reduce the poverty rate from 19% in 1964, when the war on poverty was declared, to a low of 11.1% in 1973.⁶⁸ The rate of maternal mortality declined by half, and the infant mortality rate dropped by one-third.⁶⁹ However, it is not clear what proportion

of this decrease was due to the decrease in poverty and what proportion resulted from improvements in access to and the quality of medical care. Indeed, the war on poverty fell short of its promise to address the health and social ills of society. Insufficient federal and state investments in the Medicaid program, as well as its designation as a welfare program, hindered its ability to "mainstream" the ambulatory care of the poor.⁷⁰ In addition, many of the broad-based programs designed to address comprehensive health and social needs were eventually whittled back to resemble more narrowly defined programs. For example, by 1975, funding for comprehensive health centers providing a range of medical and social services, including employment training, gave way to basic medical services without the social services and economic development components.⁷¹

Most federal efforts designed to reduce infant mortality at that time focused on improving the organization and utilization of medical services, most notably through the Improved Pregnancy Outcomes (IPO) project, funded under Title V of the Social Security Act. However, as federal investments in health and medical care were increasing, a storm of protest against public welfare was brewing and casting doubt on the effectiveness of anti-poverty programs.^{64,72} The causes of poverty were once again sought in the individual, and emphasis was placed on services to assist individuals to move out of poverty. This return to the professional services approach to poverty of the late 1920s was a distinct shift away from the cash programs of the New Deal.⁶⁴

The 1980s: Reducing Government's Role

Led by the Reagan administration, Congress during the early 1980s approved a series of actions which narrowed eligibility for Aid to Families with Dependent Children (AFDC), thereby reduced funding for health and welfare programs, and transferred authority for major maternal and child health programs to the states.⁷³ Virtually every state followed suit, further reducing the amount spent on key health and welfare programs. Among the most stark results of these actions was the sharp drop in the ratio of poor children who receive AFDC to the total number of poor children. This ratio peaked at about 80% in 1973, fell to about 50% in 1982, and then rose to about 59% in 1989.⁶⁸

The increasing evidence of stagnation in infant mortality trends during the early 1980s set the stage for the unlinking of publicly financed health insurance from welfare assistance established in the mid-1960s. For the first time, Congress in 1984 expanded eligibility for Medicaid to poor pregnant women and children who were not categorically eligible for AFDC (usually because they lived in two-parent families).⁷⁴ By breaking this link, Congress paved the way for subsequent eligibility expansions, resulting in optional coverage of pregnant women and infants with incomes up to nearly two times the federal poverty level. Between 1988 and 1991 alone, 2.6 million pregnant women and children became newly eligible for Medicaid. Simultaneously, Congress granted states the option to provide pregnant women enrolled in Medicaid additional services, such as health education, nutritional counseling, and case management, even if those services were not available to other Medicaid beneficiaries.⁷⁴

Improving Socioeconomic Status: The Impact on Low Birth Weight

Today, as in earlier years, most public policies and programs designed to produce healthier newborns in the United States have focused chiefly on two strategies: (1) improving access to health and medical care received by pregnant women and (2) mitigating the effects of disadvantage during pregnancy.²⁶ Studies evaluating these approaches have produced mixed results.

Improving Access to Care

Efforts designed to improve access to health care have also demonstrated varying levels of effectiveness. A growing body of evidence suggests that these approaches have produced mixed results. One of the most significant recent efforts to improve access to maternity care involves the Medicaid program, the single largest source of funding for health care to low-income pregnant women and the single largest payer for children's health services.

Early studies comparing low birth weight rates before and after the introduction of the Medicaid program were encouraging, and showed a clear reduction in low weight births during the 1960s. Whether or not these reductions in low birth weight were due to the Medicaid program alone, to this program in combi-

nation with other improvements in medical care, or to overall reductions in poverty still remains in question. Later expansions of Medicaid coverage during the 1980s did not produce further reductions in low birth weight.

The benefit of Medicaid coverage among low-income women in contributing to better birth outcomes than are found among women who are uninsured is demonstrated in an extensive California study conducted in the early 1980s.^{75,76} The incidence of low birth weight prior to and just after the introduction of the Medicaid program generally supports this finding by suggesting that Medicaid may have contributed in part to the decline in low birth weight that occurred in the late 1960s and early 1970s, after a slow but steady increase in the early 1960s. Such crude analyses do not account for the multitude of other factors that may be associated with the decline, including reductions in poverty, introduction of other programs (such as community health centers), or greater sophistication in the management of high-risk pregnancies.⁷⁷ However, Davis and Schoen argue that the sheer size of the Medicaid program in relation to other programs for the poor strongly suggests that Medicaid may be largely responsible for improvements in certain health conditions.⁶⁶ Others have also argued that the substantial drop in postneonatal mortality which occurred at the same time (a condition also sensitive to social influences) was likely the result of health and social investments at the time.³⁵ Further, it is clear that, with the advent of Medicaid, the numbers of poor persons with health insurance rose significantly.¹⁶ More important, instead of the poor having the lowest number of physi-

With the advent of Medicaid, the numbers of poor persons with health insurance rose significantly.

cian visits per capita, health care utilization among the poor after Medicaid rose to exceed that of middle- and upper-income groups, as would be appropriate given their greater health needs.⁷⁸

Confounding these earlier results of a positive association between Medicaid coverage and low birth weight are more re-

cent studies of the impact of later eligibility expansions for the Medicaid program. During the 1980s, eligibility for Medicaid coverage was gradually expanded for pregnant women from criteria which restricted eligibility to those also eligible for AFDC to include all pregnant women with incomes below 185% of the federal poverty line.⁷⁴ In two studies, Piper and colleagues^{79,80} found no improvements in birth outcomes from Medicaid expansion in Tennessee.⁷⁹

Such mixed results may be caused by several factors. First, the target population in earlier versus later Medicaid expansions varied considerably in terms of their risk for low birth weight. While the earlier expansions affected extremely low-income women, later expansions targeted women without health insurance but with greater resources. Indeed, the group covered by the later expansions was more likely to be white and married, slightly older, more likely to work, and less likely to receive public assistance than the group covered by the earlier expansions.⁸¹ Because the Piper studies evaluated outcomes among

women who were at less risk of poor birth outcomes, expectations of significant improvements in their rates may not be warranted.⁸²

The lack of an effect could also reflect a failure to translate expanded eligibility into actual coverage and/or genuine access to care.⁸² A study by Currie and colleagues⁸³ supports this theory by differentiating the impact on birth outcomes of early, narrowly targeted expansions in eligibility from later, more broad-based expansion efforts.⁸¹ This study found that the early expansions, such as relaxations in family structure requirements, are estimated to have resulted in a 4.5% decline in the incidence of low birth weight for every 20-percentage-point increase in the number of women eligible for Medicaid. This compared to only a 0.4% decline in the incidence of low birth weight for a similar magnitude of change in eligibility during the later, broader expansions. The authors found that the absence of effect for the broader expansion resulted largely from newly eligible women not successfully enrolling in the program. Finally, methodological concerns with constructing the appropriate linked data bases may lead to serious underascertainment of adverse outcomes.⁸⁰

Improving the Content of Prenatal Care

Providing financial access to care in the form of public insurance is only the first step toward improving birth outcomes. Providing effective prenatal care is another requisite. Studies that examine the effect of prenatal care on low birth weight have shown varying results. (See the article by Alexander and Korenbrot in this journal issue.) Prenatal care, for example, while benefitting some populations, appears to have less benefit for others.

Certain socially oriented components of prenatal care have also shown varying levels of effectiveness. Linking pregnant women to social services,⁸⁴ health education,⁸⁵ and home visiting⁸⁶ has been demonstrated to contribute to lower rates of low birth weight among high-risk women. Similarly, prenatal care programs that incorporate provision and coordination of nutrition, health education, psychosocial assessments and services have also been found to produce better results among high-risk women.^{75,76,85,87} Yet, other evaluations have suggested that some of these services are less effective.

One of the few large randomized experiments on psychosocial support found no difference in birth outcomes among high-risk pregnant women receiving four or more home visits in the final quarter of pregnancy, compared with a similar group that did not receive the visits and accompanying social support.⁸⁸ Similarly, another evaluation of social support found that this intervention failed to improve low birth weight rates.⁸⁹ While the apparent contradiction in these results may be at least partly explained by varying study designs, it also implies that the effectiveness of these approaches has yet to be fully proven.

Reducing the Effects of Poverty

It is difficult to draw conclusions about whether efforts intended to permanently improve social status are more or less beneficial than those that temporarily mitigate the influence of poverty through medical care or pregnancy-related social services. Only rarely have domestic maternal and infant health interventions been aimed at addressing the underlying sources of that disadvantage through income support, housing assistance, employment training, or other resource strategies designed to reduce or eliminate the circumstances leading to poverty. Fewer still are reliable evaluations of such resource/social strategies. However, some information is available regarding food supplementation and income support. Specifically, the most complete information is available about the Women, Infants and Children (WIC) program and about income support.

The WIC Program

The WIC program (the Special Supplemental Food Program for Women, Infants and Children), designed for low-income families at nutritional risk, combines nutritional education with vouchers for certain foods. While evaluations of the effects of the WIC program on birth outcomes have provided varying results, on balance, the majority of studies demonstrate a positive impact. It is thought that prenatal WIC participation may affect the incidence of low birth weight through the provision of food supplements and nutritional education during pregnancy. WIC participants also may receive health and social service referrals, which may result in increased use of prenatal care and other services. These referrals may also have played a role in improving the low birth weight rates among the women who participated in the WIC program.⁹⁰

Seven major studies of the effects of the WIC program have been carried out since its inception in 1972. Most of these showed either a positive effect of WIC participation on low birth weight^{91–93} or mixed results, depending on the study design.⁹⁴ A national WIC evaluation was undertaken in 1986 and found that the provision of WIC benefits did not reduce the incidence of low birth weight or preterm birth.⁹⁵ More recent studies have consistently shown that women who receive WIC benefits have lower rates of low weight births than do women of similar socioeconomic status who do not receive benefits. For example, the General Accounting Office estimates that, in 1992, women who received WIC benefits had 25% fewer low weight births and 44% fewer very low birth weight infants than did similar women

Information about the impact of resource policies on the incidence of low birth weight is far from conclusive.

who did not receive these benefits.⁹⁶ A study on the savings in Medicaid costs from WIC in five states indicated that prenatal WIC participation was associated with increased birth weight, longer gestational age, a lower incidence of low birth weight, and a lower incidence of preterm birth than were found among women on Medicaid who did not participate in the WIC program.⁹⁷

Providing Income Support

Information about the impact of resource policies on the incidence of low birth weight is far from conclusive. Not only have the extremely limited studies produced somewhat mixed results, but there simply is not enough information available to make a reliable assessment. This lack of information reflects both the paucity of research on this subject and, what is more important, the historical and ongoing failure to make the research link between health and social policy.

Few studies have examined the effect of social policies on birth weight using nationally representative data. Some observers have suggested that the high rate of low birth weight among AFDC beneficiaries is evidence that AFDC contributes to poor birth outcomes by providing low-income families with the means to pursue

unhealthy behaviors.⁹⁸ However, in a study examining the relationship between a mother's participation in AFDC during pregnancy and the birth weight of her child, Currie and colleagues found that the association disappears with appropriate modeling.⁸³ The authors suggest that, to the extent that a relationship exists, it is not a causal one. However, the authors also did not find any significant effects of AFDC participation on low birth weight

Few efforts designed to improve pregnancy outcomes have attempted to address directly insufficient resources and limited income.

and postulate that this lack of effect may be related to AFDC payment levels, which may be too small to have a direct effect on birth weight.

Other studies have found a positive relationship between income support and decreased low birth weight. In one ecological study, increased rates of late and no prenatal care and low birth weight among low-income women were correlated with economic stress during the recession of 1986 to 1991.⁹⁹ One of the few studies that examined the impact of income support on low birth weight found an average maternal weight gain of about 0.3 to 1.2 pounds in response to income intervention.¹⁰⁰ Based on additional exploratory investigations, the authors suggest that improvements in nutrition may have been part of the causal mechanism responsible for the observed response.

Future Trends

Both health care reform and welfare reform top the agendas of the Clinton administration and Congress at present. Depending on the course each reform strategy takes, they could result in meaningful improvements in the health of women and children. However, the primary debates on health care reform have not broken from the paradigm of medical solutions to problems which often stem from social roots. Discussions surrounding income security are likewise narrowly focused. Rather than concentrating on the health and resource needs of families, most proposals related to "welfare reform" seek to reduce the numbers of AFDC bene-

ficiaries and the duration of eligibility. In keeping with earlier periods, strong emphasis is placed on "making work pay," as well as on imposing incentives and penalties as a means of addressing the perceived "behavioral" determinants of poverty.¹⁰¹

Health care reform and welfare reform are strategically linked, however. By providing universal insurance coverage, even among those employed part-time or in small firms, health care reform is seen by its proponents as necessary to facilitate movement off welfare, entry into the workplace, and self-sufficiency. The current debate recognizes the fact that, without fundamental reform in the organization and financing of health care, families face the threat of financial ruin if confronted with a serious medical condition, thus linking health care reform with economic security. However, the converse is not yet true. The importance of economic security to improved health status remains absent from the current debates.

Conclusion and Recommendations

The association between socioeconomic factors and low birth weight is well established, though the precise mechanism by which these factors influence birth outcomes is not fully understood. Despite this well-known association, few efforts designed to improve pregnancy outcomes have attempted to address directly insufficient resources and limited income. Even during periods in twentieth-century American history in which social reform efforts flourished, the link between pregnancy and economic disadvantage was rarely made and never sustained.

In many respects, this separation of health and social policies is a uniquely American phenomenon. Nearly every Western European country long ago established broad-based family policies that integrate health and social strategies.¹⁰² Efforts in this country to replicate these policies, even modestly, have largely failed because of certain dominant attitudes. Indeed, the continued detachment of health and social policies in low birth weight prevention, in the face of mounting evidence of the significant role social conditions play in birth outcomes, reflects several American attitudes toward poverty, social class, and health.

Economic disadvantage continues to be viewed as more of an individual trait than the result of circumstances or patterns of social policies or political practices. People who hold this view believe that individuals must overcome their disadvantage through individual means and that society's responsibility, if any, should be limited to helping them cope through the provision of direct services. This view reflects a strong value placed on work and a reluctance to provide direct cash relief to individuals because doing so may undermine their motivation to work.¹⁰² This view creates a paradox for pregnant women for whom entering the workplace can be extremely difficult and for single-parenting women for whom work is impossible without other support such as child care and health insurance.

Yet, as the history of social reform and attention to pregnancy outcomes demonstrates, these competing notions have never been reconciled. Indeed this focus on individuals is also reflected in health care policies where remedies tend to be based on individuals rather than on communities or populations. As such, efforts are focused on services for individuals, such as use of medical technology for high-risk women, rather than being designed to reduce that risk more generally among the populations within which it exists. Thus, optimal strategies to improve pregnancy outcomes should include preventive efforts targeted to both the individual and the community.

Despite this legacy, stagnating low birth weight rates in this country suggest that a more coordinated strategy incorporating both social and medical interventions is warranted. Comprehensive prenatal care will likely be a central feature of this strategy, even if its effectiveness is limited to certain groups. However, more should be done to address the various resource-related problems that contribute to poverty and its associated health problems.¹⁰²

To do so will require changes on the part of both researchers and policymakers. As a first step, both must embrace a broader definition of health which incorporates social dimensions. Unless the scope of health problems is viewed within a broader context, the range of questions and remedies is likely to be limited to those traditionally undertaken. On the other hand, a more comprehensive view of health would allow for an appropriate

blending of theoretical frameworks and methodologies from social sciences into health and medical research, as well as permit consideration of strategies that unite the health and social components of the low birth weight equation. Similarly, the focus of research and interventions should be recast from pregnancy outcomes and infant health exclusively to one that embraces the notion of women's health more globally. This focus on women's health may lead to more effective strategies by incorporating women's health status prior to conception, as well as during and after pregnancy, thereby increasing both the time frame and the range of interventions that may be introduced. Such an approach also permits a more comprehensive view of the contextual factors that contribute to pregnancy outcomes, such as health status at the time of pregnancy, health habits and behaviors, and use of health services.

Beyond these initial steps, there is a need for an expanded research agenda to unravel the paradox of socioeconomic factors and health. This requires routinely collecting socioeconomic data related to individuals, families, and communities in health-related surveys. It also requires

Optimal strategies to improve pregnancy outcomes should include preventive efforts targeted to both the individual and the community.

more research which attempts to identify the specific mechanisms by which socioeconomic status influences low birth weight so that more refined measures of social class may be developed and used. Further, studies are needed which specifically explore the impact of income and other resource interventions on low birth weight. Collaborations with other countries where national family policies guarantee income security for families may provide a promising start.

Ultimately, however, the nation's persistently high rate of low birth weight would be most effectively addressed through a dedicated, national commitment to assuring adequate support to individuals and families, including ample income and health care. Sufficient evidence is available to point to significant health

benefits of an integrated approach to health and well-being, incorporating high-quality medical care with protections against poverty and its circumstances. Given historical precedent and countervailing cultural pressures, achievement of this goal will not be easy. However, as this nation approaches the limits of medical and service interventions, in terms of both what they can accomplish and what they cost, alternatives will be required. Meanwhile, successful completion of additional

research conducted in this country to further document the value of integrated social and health policies will be useful. More immediately, the nation is again at a critical juncture where efforts to address health and social issues are under way simultaneously. This convergence presents another opportunity to examine the relationship between health and socioeconomic conditions and to develop an integrated policy of health and economic security.

1. Rogers, R.G. Living and dying in the USA: Sociodemographic determinants of death among blacks and whites. *Demography* (May 1992) 29,2:287–303.
2. Kaplan, G.A., Haan, M.N., Syme, S.L., et al. Socioeconomic status and health. In *Closing the gap: The burden of unnecessary illness*. R.W. Amer and H.B. Dull, eds. New York: Oxford University Press, 1987, pp. 125–29.
3. Marmot, M.G., Adelstein, A.M., Robinson, N., and Rose, G.A. Changing social-class distribution of heart disease. *British Medical Journal* (1978) 1:1109–12.
4. Syme, L.S., and Berkman, L.F. Social class, susceptibility and sickness. *American Journal of Epidemiology* (1976) 104:1–8.
5. Antonovsky, A. Social class, life expectancy and overall mortality. *Milbank Memorial Fund Quarterly* (1967) 45:31–73.
6. Devesa, S.S., and Diamond, E.L. Association of breast cancer and cervical cancer incidence with income and education among whites and blacks. *Journal of the National Cancer Institute* (1980) 65:515–28.
7. Horon, I.L., Strobino, D.M., and MacDonald, H.M. Birth weights among infants born to adolescent and young adult women. *American Journal of Obstetrics and Gynecology* (1983) 146:444–49.
8. Paneth, N., Wallenstein, S., Kiely, J., and Susser, M. Social class indicators and mortality in low birth weight infants. *American Journal of Epidemiology* (1982) 116,2:364–75.
9. Liberman, E., Ryan, K., Monson, R., et al. Risk factors accounting for racial differences in the rate of premature birth. *New England Journal of Medicine* (1987) 317:743–48.
10. Elbourne, D., Prichard, C., and Dauncey, M. Perinatal outcomes and related factors: Social class differences within and between geographic areas. *Journal of Epidemiology and Community Health* (1986) 40:301–8.
11. Berkowitz, G.S. An epidemiological study of preterm delivery. *American Journal of Epidemiology* (1981) 113:81–92.
12. Erickson, A., Eriksson, M., and Setterstrom, R. Analysis of perinatal mortality in the Stockholm area. *Acta Paediatrica Scandinavica Supplement* (1979) 276:35–40.
13. Frederik, J., and Adelstein, P. Factors associated with low birthweight of infants delivered at term. *British Journal of Obstetrics and Gynaecology* (1978) 85:1–11.
14. Susser, M., Watson, W., and Hopper, K. *Sociology in medicine*. New York: Oxford University Press, 1985.
15. Kitagawa, E.M., and Hauser, P.M. *Differential mortality in the United States: A study in socioeconomic epidemiology*. Cambridge, MA: Harvard University Press, 1973.
16. Luft, H.S. *Poverty and health: Economic causes and consequences of health problems*. Cambridge, MA: Ballinger, 1978.
17. Marmot, M.G., Shipley, M., and Rose, G. Inequalities in death—Specific explanations of a general pattern. *Lancet* (May 5, 1984) 1:1003–6.
18. Rose, G., and Marmot, M.G. Social class and coronary heart disease. *British Heart Journal* (1981) 45,1:13–19.
19. U.S. Department of Health and Human Services. *Health status of minorities and low-income groups*. 3rd ed. Washington, DC: U.S. Government Printing Office, 1991.

20. Haan, M., and Kaplan, G. The contribution of socioeconomic position to minority health. In *Report of the Secretary's Task Force on Black and Minority Health*. Vol. 2. Washington, DC: U.S. Department of Health and Human Services, 1986, pp. 69–103.
21. Adler, N.E., Boyce, W.T., Chesney, M.A., et al. Socioeconomic inequalities in health: No easy solution. *Journal of the American Medical Association* (1993) 269,24:3140–45.
22. Johnson, J.W.C., and Dubin, N.H. Prevention of preterm labor. *Clinical Obstetrics and Gynecology* (1980) 23:51–73.
23. Antonovsky, A., and Bernstein, J. Social class and infant mortality. *Social Science and Medicine* (1977) 11:453–70.
24. Murrells, T.J., Catford, J.C., Smith, T.M.F., and Machin, D. The use of logit models to investigate social and biological factors in infant mortality. II: Stillbirths. *Statistics in Medicine* (1985) 4:189–200.
25. Collins, J.W., and David, R.J. The differential effect of traditional risk factors on infant birthweight among blacks and whites in Chicago. *American Journal of Public Health* (1990) 80:679–81.
26. Institute of Medicine, Committee to Study the Prevention of Low Birthweight. *Preventing low birthweight*. Washington, DC: National Academy Press, 1985.
27. McCormick, M.C. The contribution of low birth weight to infant mortality and childhood morbidity. *New England Journal of Medicine* (1985) 312:82–90.
28. Gortmaker, S.L. The effects of prenatal care upon the health of the newborn. *American Journal of Public Health* (1979) 69,7:653–60.
29. van den Berg, B.J., and Oechsli, F.W. Prematurity. In *Perinatal epidemiology*. M.B. Bracken, ed. New York: Oxford University Press, 1984, pp. 69–85.
30. Fedrick, J., and Anderson, A.B.M. Factors associated with spontaneous preterm birth. *British Journal of Obstetrics and Gynaecology* (1976) 83:342–50.
31. Fedrick, J., and Adelstein, P. Factors associated with low birth weight of infants delivered at term. *British Journal of Obstetrics and Gynaecology* (1978) 85:1–11.
32. Kieffer, E.C., Alexander, G.R., Lewis, N.D., and Mor, J. Geographic patterns of low birthweight in Hawaii. *Social Science and Medicine* (1993) 36,4:557–64.
33. Gould, J.B., and LeRoy, S. Socioeconomic status and low birth weight: A racial comparison. *Pediatrics* (1988) 82:896–904.
34. Ounsted, M., and Scoll, A. Social class and birthweight: A new look. *Early Human Development* (1982) 6:83–89.
35. Starfield, B., and Budetti, P. Child health status and risk factors. *Health Services Research* (1985) 19,6:817–86.
36. Newacheck, P.W. Access to ambulatory care for poor persons. *Health Services Research* (1988) 23,3:401–19.
37. Klerman, L. *Alive and well? A research and policy review of health programs for poor young children*. New York: National Center for Children in Poverty, Columbia University, 1991.
38. Kramer, M.S. Intrauterine growth and gestational duration determinants. *Pediatrics* (1987) 80,4:502–11.
39. Stein, Z., and Kline, J. Smoking, alcohol and reproduction. *American Journal of Public Health* (1983) 73,10:1154–56.
40. Rush, D., and Cassano, P. Relationship of cigarette smoking and social class to birthweight and perinatal mortality among all births in Britain, 5–11 April 1970. *Journal of Epidemiology and Community Health* (1983) 37:249–55.
41. Pamuk, E.R., and Mosher, W.D. *Health aspects of pregnancy and childbirth: United States, 1982*. Vital and Health Statistics, Series 23, No. 16. Hyattsville, MD: National Center for Health Statistics, 1993.
42. U.S. General Accounting Office. *Drug-exposed infants: A generation at risk*. Statement of the Comptroller General of the United States before the U.S. Senate, Committee on Finance. Washington, DC: GAO, 1990.
43. Chasnoff, I., Landress, H.J., and Barnett, M.E. The prevalence of illicit drug or alcohol use during pregnancy and discrepancies in mandatory reporting in Pinellas County, Florida. *New England Journal of Medicine* (1990) 322,17:1201–6.
44. Frank, D.A., Zuckerman, B.S., Amaro, H., et al. Cocaine use during pregnancy: Prevalence and correlates. *Pediatrics* (1988) 82,6:888–95.

45. Williams, D.R. Socioeconomic differentials in health: A review and redirection. *Social Psychology Quarterly* (1990) 53,2:81–99.
46. U.S. Department of Health and Human Services. *Report of the Secretary's Task Force on Black and Minority Health*. Vol 1: Executive summary. Washington, DC: DHHS, 1985.
47. U.S. Bureau of the Census. *Statistical Abstract of the United States: 1992*. Washington, DC: U.S. Government Printing Office, 1992.
48. Kleinman, J.C., and Kessel, S.S. Racial differences in low birth weight: Trends and risk factors. *New England Journal of Medicine* (1987) 317:749–53.
49. Starfield, B., Shapiro, S., Weiss, J., et al. Race, family income and low birthweight. *American Journal of Epidemiology* (1991) 134,10:1167–74.
50. Shiono, P.H., Klebanoff, M.A., Graubord, B.L., et al. Birth weight among women of different ethnic groups. *Journal of the American Medical Association* (1986) 255:48–52.
51. Spurlock, C.W., Hinds, M.W., Skaggs, J.W., and Hernandez, C.E. Infant death rates among poor and non-poor in Kentucky, 1982–1983. *Pediatrics* (1987) 80:262–69.
52. Kreiger, N. Racial and gender discrimination: Risk factors for high blood pressure? *Social Science Medicine* (1990) 30:1273–81.
53. Haan, M.N., Kaplan, G.A., and Syme, S.L. Socioeconomic status and health: Old observations and new thoughts. In *Pathways to health: The role of social factors*. J.P. Bunker, D.S. Gomby, and B.H. Kehrner, eds. Palo Alto, CA: Henry J. Kaiser Foundation, 1989, pp. 76–133.
54. House, J.S., Landis, K.R., and Umberson, D. Social relationships and health. *Science* (1988) 241:540–45.
55. Meckel, R. *Save the babies*. Baltimore, MD: Johns Hopkins University Press, 1991.
56. Lesser, A.J. The origin and development of maternal and child health programs in the United States. *American Journal of Public Health* (1985) 75:590–98.
57. Guyer, B. The evolution and future role of Title V. In *Children in a changing health system: Assessments and proposals for reform*. M. Schlesinger and L. Eisenberg, eds. Baltimore, MD: Johns Hopkins University Press, 1990, pp. 297–324.
58. Starfield, B.J. Giant steps and baby steps: Toward child health. *American Journal of Public Health* (1985) 75:599–604.
59. Klerman, L., Russell, A.Y., and Valadian, I. *Promoting the health of women and children through planning*. Washington, DC: Maternal and Child Health Bureau, U.S. Department of Health and Human Services, 1982.
60. Skocpol, T. *Protecting soldiers and mothers: The political origins of social policy in the United States*. Cambridge, MA: Harvard University Press, 1993.
61. Zelitzer, V.A. *Pricing the priceless child: The changing social value of children*. New York: Basic Books, 1985.
62. Buhler-Wilkinson, K. Bringing care to the people: Lillian Wald's legacy to public health nursing. *American Journal of Public Health* (1993) 83,12:1773–77.
63. Kamerman, S.B. Toward a child policy decade. *Child Welfare* (1989) 1018,4:371–90.
64. Axinn, J., and Levin, H. *Social welfare: A history of the American response to need*. 2d ed. New York: Harper & Row, 1982.
65. Schmidt, W. How children got into the act. In *Children and youth in America*. Vol. 3: 1933–1973, Parts 5 through 7. R.H. Bremner, ed. Cambridge, MA: Harvard University Press, 1974, p. 1211.
66. Davis, K., and Schoen, C. *Health and the war on poverty: A ten year appraisal*. Washington, DC: Brookings Institution, 1978.
67. Preston, S.H. Children and the elderly in the United States. *Scientific American* (1984) 251,6:44–49.
68. Danziger, S.H., Sandefur, G.D., and Weinberg, D.H. The historical record: Trends in family income, inequality, and poverty. In *Confronting poverty: Prescriptions for change*. Cambridge, MA: Harvard University Press, 1994, pp. 18–50.
69. National Center for Health Statistics. *Advance report of final mortality statistics, 1989*. Monthly Vital Statistics Report, Vol. 40, No. 8, Suppl. 2. Hyattsville, MD: Public Health Service, 1992.
70. Starr, P. *The social transformation of American medicine*. New York: Basic Books, 1984.
71. Sardell, A. Child health policy in the U.S.: The paradox of consensus. *Journal of Health Politics, Policy and Law* (Summer 1990) 15,2:271–304.
72. Burtless, G. Public spending on the poor: Historical trends and economic limits. In *Confronting poverty: Prescriptions for change*. Cambridge, MA: Harvard University Press, 1994, pp. 51–84.

73. Hughes, D., Johnson, K., Rosenbaum, S., et al. *The health of America's children: The maternal and child health data book*. Washington, DC: Children's Defense Fund, 1988.
74. Feder, J., Rowland, D., Holahan, J., et al. *The Medicaid cost explosion: Causes and consequences*. Baltimore, MD: Henry J. Kaiser Family Foundation, 1993.
75. Korenbrot, K.C. Risk reduction in pregnancies of low income women. *Mobius* (1984) 4,3:34–43.
76. Lennie, J.A., Klun, J.R., and Hausner, T. Low birthweight rate reduced by the Obstetrical Access Project. *Health Care Financing Review* (1984) 8,3:83–86.
77. Cramer, J. Social factors and infant mortality: Identifying high risk groups and proximate causes. *Demography* (1987) 24,3:299–322.
78. Marmor, T.R., and Monroe, J.A. The health programs of the Kennedy-Johnson years: An overview. In *Towards new human rights: The social policies of the Kennedy and Johnson administrations*. D.C. Warner, ed. Austin, TX: LBJ School of Public Affairs, 1977, pp. 157–82.
79. Piper, J.M., Mitchel, Jr., E.F., and Ray, W.A. Expanded Medicaid coverage for pregnant women to 100% of the federal poverty level. *American Journal of Preventive Medicine* (1994) 10,2:97–102.
80. Piper, J., Ray, W., Griffin, M., et al. Methodological issues in evaluating expanded Medicaid coverage for pregnant women. *American Journal of Epidemiology* (1990) 132,3:561–71.
81. Currie, J., and Gruber, J. *Saving babies: The efficacy and cost of recent expansions of Medicaid eligibility for pregnant women*. Working Paper No. 4644. Cambridge, MA: National Bureau of Economic Research, 1994.
82. Guyer, B. Medicaid and prenatal care: Necessary but not sufficient. *Journal of the American Medical Association* (1990) 264,17:2264–65.
83. See note no. 81, Currie and Gruber, for more information on recent Medicaid eligibility expansions for pregnant women.
84. Alexander, G.R., Weiss, J., Hulsey, T.C., and Papiernik, E. Preterm birth prevention: An evaluation of programs in the United States. *Birth* (1991) 18,3:160–69.
85. McLaughlin, F.J., Altemeier, W.A., Christensen, M.J., et al. Randomized trial of comprehensive prenatal care for low income women: Effect on low birth weight. *Pediatrics* (1992) 89,1:128–32.
86. Olds, D.L., and Kitzman, H. Review of research on home visiting for pregnant women and parents of young children. *The Future of Children* (Winter 1993) 3,3:53–92.
87. Buescher, P.A., Goforth, C.M., Roth, M.S., and Williams, D. An evaluation of the impact of maternity care coordination on Medicaid birth outcomes in North Carolina. *American Journal of Public Health* (1991) 81,12:1625–29.
88. Villar, J., Farnot, U., Barros, F., et al. A randomized trial of psychosocial support during high risk pregnancies. *New England Journal of Medicine* (1992) 327,18:1266–71.
89. Oakly, A., Rajan, L., and Grant, A. Social support and pregnancy outcome. *British Journal of Obstetrics and Gynaecology* (1990) 97:155–62.
90. Devaney, B. *Very low birthweight among Medicaid newborns in five states. The effects of prenatal WIC participation: Volume 2*. Washington, DC: U.S. Department of Agriculture, Food and Nutrition Service, September 1992.
91. Kennedy, E.T., Gerhoff, S., Reed, R., and Austin, J.E. Evaluation of the effect of WIC supplemental feeding on birth weight. *Journal of the American Dietetic Association* (1982) 80:220–27.
92. Kotelchuck, M., Schwartz, J.B., Anderka, M.T., and Finison, K.S. WIC participation and pregnancy outcomes: Massachusetts statewide evaluation project. *American Journal of Public Health* (1984) 74,10:1086–1148.
93. Metcalf, J., Costiloe, P., and Crosby, W.M. Effect of food supplementation (WIC) during pregnancy on birthweight. *American Journal of Clinical Nutrition* (1985) 41:933–47.
94. Stockbauer, J.W. Evaluation of the Missouri WIC program: Prenatal components. *Journal of the American Dietetic Association* (1986) 86,1:61–67.
95. Rush, D. Evaluation of the Special Supplemental Food Program for Women, Infants and Children. *American Journal of Clinical Nutrition Supplement* (1988) 48,2:512–19.
96. U.S. General Accounting Office. *Early intervention: Federal investments like WIC can produce savings*. GAO/HRD-92-18. Washington, DC: GAO, 1992.
97. Devaney, B., Bilheimer, L., and Schore, J. *The savings in Medicaid costs for newborns and their mothers from prenatal participation in the WIC program: Volume 1*. Washington, DC: U.S. Department of Agriculture, Food and Nutrition Service, October 1990.
98. Murray, C. *Losing ground: American social policy, 1950–1980*. New York: Basic Books, 1984.

99. Fisher, E.S., LoGerfo, J.P., and Darling, J.R. Prenatal care and pregnancy outcomes during the recession: The Washington state experience. *American Journal of Public Health* (1985) 75,8:866–96.
100. Kehrer, B.H., and Wolin, C.M. Impact of income maintenance on low birthweight: Evidence from the Gary Experiment. *Journal of Human Resources* (1978) 14,4:432–61.
101. Rector, R. Strategies for welfare reform. (Hearing before the U.S. Congress, House, Domestic Task Force of the Select Committee on Hunger.) In *Federal policy perspectives on welfare reform: Rhetoric, reality, and opportunities*. Hearing, April 9, 1992 (Serial No. 102-25). Washington, DC: U.S. Government Printing Office, 1992, pp. 60–89.
102. Kamerman, S.B. Child care policies and programs: An international overview. *Journal of Social Issues* (1991) 47,2:179–96.

The Role of Prenatal Care in Preventing Low Birth Weight

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Abstract

Prenatal care has long been endorsed as a means to identify mothers at risk of delivering a preterm or growth-retarded infant and to provide an array of available medical, nutritional, and educational interventions intended to reduce the determinants and incidence of low birth weight and other adverse pregnancy conditions and outcomes. Although the general notion that prenatal care is of value to both mother and child became widely accepted in this century, the empirical evidence supporting the association between prenatal care and reduced rates of low birth weight emerged slowly and has been equivocal. Much of the controversy over the effectiveness of prenatal care in preventing low birth weight stems from difficulties in defining what constitutes prenatal care and adequate prenatal care use. While the collective evidence regarding the efficacy of prenatal care to prevent low birth weight continues to be mixed, the literature indicates that the most likely known targets for prenatal interventions to prevent low birth weight rates are (1) psychosocial (aimed at smoking); (2) nutritional (aimed at low prepregnancy weight and inadequate weight gain); and (3) medical (aimed at general morbidity). System level approaches to impact the accessibility and the appropriateness of prenatal health care services to entire groups of women and populationwide health promotion, social service, and case management approaches may also offer potential benefits. However, data on the effectiveness of these services are lacking, and whether interventions focused on building cohesive, functional communities can do as much or more to improve low birth weight rates as individualized treatments has yet to be explored. The ultimate success of prenatal care in substantially reducing current low birth weight percentages in the United States may hinge on the development of a much broader and more unified conception of prenatal care than currently prevails. Recommendations for actions to maximize the impact of prenatal care on reducing low birth weight are proposed both for the public and for the biomedical, public health, and research communities.

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Prenatal care has long been endorsed as a means to identify mothers at risk of delivering a preterm or growth-retarded infant and to provide an array of available medical, nutritional, and educational interventions intended to reduce the risks of low birth weight and other adverse pregnancy conditions and outcomes. In both Europe and the United States, an increasing interest in the beneficial role of prenatal care was evident from the beginning of this century and

has continued to date.^{1,2} In the late 1800s, the content of prenatal care and the timing and frequency of visits were initially developed to detect a rare but potentially life-threatening illness—eclampsia—which results in high blood pressure, convulsions, and potentially death.³ Regular screening of the mother's urine and blood pressure was routinely incorporated into prenatal care to detect the occurrence of this disease.^{2,4}

In 1901, organized outpatient prenatal care in the United States was reported and consisted of home visits performed by social reformers and nurses.^{2,3} The purpose of these visits was to provide instruction in self-care and emotional support for low-income women.^{2,3} Eighty-four years later, the enrollment of all pregnant women in a system of prenatal care was promoted as a national policy to reduce the risk of low birth weight.⁵ In spite of this national recognition of the importance of prenatal care, considerable ambiguity still exists regarding its content and efficacy.⁶

Today, the content of prenatal care varies but typically is initiated in the first trimester of pregnancy and has an increasing schedule of visits as the pregnancy progresses. If a woman's pregnancy goes to term, she may typically have anywhere from 10 to 14 prenatal visits. The content of this care usually includes screening for a variety of medical conditions, physical exams, and ancillary educational or coun-

ability of this intervention and the difficulties inherent in measuring the adequacy of its use and its content. Prenatal care has many aspects including, at a minimum, when it starts, the number and spacing of the visits, the content of each visit, the type of provider, the provider setting (for example, hospital, clinic, or home), the assessment of risk status, the schedule of medical screening tests, and the use of specific medical, educational, nutritional, and social support intervention services. The history of efforts to assess the impact of prenatal care documents the dogged determination of several generations of investigators to define and evaluate a complex and changing intervention with numerous components while being generally limited to the use of observational studies.

The collective evidence suggests that adequate prenatal care is associated with reduced rates of low birth weight but mainly among more mature full-term infants. Unfortunately, prenatal care has consistently not been shown to prevent fetal growth retardation among less mature preterm infants or to prevent preterm birth.⁷ The relationship between prenatal care and very low birth weight (less than 1,500 grams, or 3 pounds, 5 ounces) and very preterm delivery (at less than 33 weeks) is also uncertain. Programs established to prevent the onset of preterm labor and to facilitate its early identification and treatment also did not clearly reduce rates of preterm birth or low birth weight.⁸⁻¹⁰ These generally negative results underscore the lack of well-defined programmatic approaches currently available to prenatal care providers to prevent preterm birth.^{8,11}

The results of randomized controlled trials that have attempted to evaluate differences in birth outcomes between standard prenatal care and more comprehensive medical, nutritional, educational, and psychosocial support service configurations have also been generally negative, although some have shown benefits for specific populations.^{10,12-15} A comprehensive program of prenatal nurse home visiting had no overall effect on birth

In spite of this national recognition of the importance of prenatal care, considerable ambiguity still exists regarding its content and efficacy.

selling services. Providers who serve very-low-income populations often assist women to enroll in Medicaid and refer them to public and private food supplementation programs and other social services.

The Impact of Prenatal Care on Low Birth Weight

Although the general notion that prenatal care is of value to both mother and child became widely accepted during the twentieth century, the empirical evidence supporting the association between prenatal care and reduced rates of low birth weight emerged slowly and has been equivocal. The slow pace of research in this area reflects, in part, the complexity and vari-

weight or gestational age, but improvements in birth weight were noted for specific subgroups of women, for example, young adolescents.¹²

A prenatal intervention provided by nurse-midwives which included patient education, social support, and nutritional and substance-use counseling also resulted in no differences in low birth weight from programs in which obstetricians provided only usual care.¹⁰ In other studies, the addition of social support or enhanced prenatal care services also failed to reduce rates of low birth weight.^{13–16}

Although the combined evidence from nonrandomized studies suggests a relationship between some prenatal care services and mean or low birth weight, the many threats to validity of inference inherent in these nonrandomized studies need appraisal.^{17–30} Nonrandomized observational studies do not control for the self-selection bias of women who may choose to use comprehensive rather than standard services. Further, if participation in a comprehensive prenatal care program is determined by the receipt of a minimum number of visits, gestational age must be considered as a potential confounder in the selection of a comparison group.

There is little definitive information on the extent to which specific individual components or some combination of components of standard or comprehensive prenatal care—for example, social support, home visits, education, and the like—may be effective.

A recent study, examining the relationship between the receipt of a recommended array of initial medical procedures and health promotional advice during prenatal care and low birth weight reported a positive benefit for health advice but no associated impact for the initial medical procedures.³¹ Variations by provider in the content of prenatal care have been noted, and there is mounting evidence that these variations may exist among population subgroups in the content of prenatal care they received.^{32–36}

As many of these studies relied on mothers' memory of the advice and care that they received, the possibility of recall bias must be considered in the interpretation of these results.

Problems in Defining the Relationship Between Prenatal Care and Low Birth Weight

Defining an accurate way to measure the adequacy of prenatal care has been a major challenge. Over the years, it has been defined by the number of visits, the stage of pregnancy at which care was initiated, the source of care (private versus clinic, public, or ward), the spacing of visits, and/or the content of medical care and auxiliary services (for example, blood and urine tests, health education, and dental care).^{37–41} In 1962, Shwartz suggested that the association between low birth weight and the trimester in which care began or the number of prenatal care visits may well be confounded by gestational age.⁴² Mothers who delayed initiation of care until the third trimester are likely to have a declin-

Defining an accurate way to measure the adequacy of prenatal care has been a major challenge.

ing risk of low birth weight as they are approaching full term when care begins. Conversely, increased birth weight may be expected to coincide with more visits because both birth weight and the total number of scheduled visits increase with gestational age. The importance of adjusting for the effects of gestational age when relating prenatal care use to birth weight has now been recognized by many investigators.^{7,42–45}

The cumulative results of studies of adequate prenatal care utilization indices have had a dramatic influence on establishing a widespread confidence in the ability of early and frequent use of prenatal care to reduce the risk of low birth weight.^{45–47} Nevertheless, limitations to these studies have been recognized. Self-selection bias is a major concern in the interpretation of research in this area.^{5,43,46,47} Health-conscious women may be more likely to initiate prenatal care early and to maintain a regular schedule of visits. These same women may also demonstrate other health-care-seeking and health-promoting behaviors, including planning their pregnancies, obtaining preconceptional care, maintaining a

Table 1

Use of Prenatal Care by Birth Weight for Single Live Births to U.S.–Resident Mothers, 1986 (3,670,676 births)							
	Use of Prenatal Care Categories						
	Adequate	Intermediate	Inadequate	No Care	Missing	Total	
	Percentage of Prenatal Care Use						
All infants	55.64	19.15	5.14	1.87	18.20	100	
Low birth weight infants	42.41	23.49	7.76	5.69	20.66	100	
	Percentage of Birth Weight Category						
	Very low birth weight (<1,500 grams)	0.70	1.02	0.90	5.16	1.55	1.02
	Moderately low birth weight (1,500–2,499 grams)	3.75	6.15	7.85	12.66	5.08	4.83
	Low birth weight (< 2,500 grams)	4.45	7.17	8.82	17.82	6.63	5.85

Source: National Center for Health Statistics. (1991). *Linked birth and infant death data set: 1986 birth cohort*. (Data tape.) Available: Mortality Statistics Branch, Division of Vital Statistics, NCHS, Centers for Disease Control and Prevention, 6525 Belcrest Rd., Rm. 840, Hyattsville, MD 20782, (301) 436-8884.

proper diet, and abstaining from the use of tobacco, alcohol, and illicit substances. They may influence the content of their care through their selection of a prenatal care provider and through their requests for and adherence to provider advice on positive pregnancy-related behaviors. These health-promoting behaviors may contribute to reducing the risk of a low birth weight delivery. Hence, adequacy of prenatal care use could be an indicator of myriad health-enhancing maternal attitudes and behaviors as well as a measure of the prenatal care received. In the absence of findings from randomized controlled trials, this unaddressed self-selection bias leaves concerns as to whether simply improving the adequacy of prenatal care use will result in improvements in low birth weight.

There are other limitations to studies of prenatal care use. It should be noted that prenatal care utilization indices, which combine the timing of initiation and the number of visits, are unable to assess these components of the index separately or to address issues related to the content of the services received. (The two-part adequacy of prenatal care utilization index proposed by Kotelchuck, which

separately assesses initiation and adequacy of visits, is a notable exception.⁴⁸) Finally, lack of clarity still exists regarding some of the mechanisms or biological pathways by which prenatal care services influence low birth weight and its specific components of preterm and small-for-gestational-age birth. In more recent studies, researchers have found that the major impact of any prenatal care use on birth weight is limited to more gestationally mature infants.^{49,50}

To illustrate the general findings of studies using adequacy of prenatal care indices, Table 1 presents birth weight characteristics by adequacy of prenatal care utilization groups for 1986 single live births to U.S.-resident mothers.⁵¹ Prenatal care utilization categories were defined using a modified version of the Kessner index.^{45,46} The majority of mothers (56%) demonstrated adequate utilization, and less than 7% reported inadequate utilization or no care. Among mothers of low birth weight infants, 42% adequately utilized prenatal care, while 13.5% exhibited inadequate or no prenatal care use.

The second section of the table provides low birth weight percentages for each category of prenatal care use. The

moderately low (1,500 to 2,499 grams, or between 3 pounds, 5 ounces and 5 pounds, 8 ounces) birth weight percentages progressively increased with less than adequate prenatal care utilization (3.75% for adequate to 7.85% for inadequate). A similar progressive relationship between adequacy of prenatal care and very low birth weight (less than 1,500 grams) was not in evidence, however. It should be emphasized that the very low birth weight category is appreciably comprised of very preterm infants, a condition for which there is less evidence of a relationship with prenatal care use. While these data appear to demonstrate an association between adequacy of care and moderately low birth weight, they are fraught with most of the problems noted above and, thus, cannot be viewed as definitive.

Ways in Which Prenatal Care Services Might Impact Low Birth Weight Deliveries

For prenatal care to prevent low birth weight deliveries, women at risk of giving birth to preterm or intrauterine growth-retarded infants need to be identified in an accurate and timely manner and to receive effective interventions to reduce preventable risks. Unfortunately, the high risk assessment screening systems that are currently available are neither sensitive nor specific enough to be of great clinical value.^{5,8} Further, many incorporate risk factors that are immutable, for example, ethnicity, which limits the potential impact of prevention-oriented prenatal care efforts aimed at modifying amenable risk characteristics.⁸ To appraise the potential impact of universal access and use of prenatal care on reducing the current rates of low birth weight, we must consider the degree to which the currently known determinants of low birth weight and its sub-components, preterm delivery and intrauterine growth retardation, are potentially preventable or mutable. This needs to be done to estimate a low birth weight percentage that is likely to be achieved through prenatal care interventions. One approach for estimating this target is to determine the proportion of the low birth weight problem in a population which is potentially modifiable.

Establishing the relative prevalence and strength of the known precursors of

intrauterine growth retardation (IUGR) and preterm birth is difficult because so little is known about their direct causes.⁵²⁻⁵⁴ In developed countries, the predominant risk factors in order of importance are: (1) cigarette smoking; (2) low maternal weight gain; (3) low prepregnancy weight; (4) first births; (5) female sex; (6) short maternal stature; (7) black race/ethnicity; (8) maternal low birth weight and prior low birth weight history; and (9) general morbidity.⁵²⁻⁵⁴ The top three risk factors can potentially be modified and have been suggested to be involved in nearly two-thirds of IUGR births. Although these estimates suggest that we have a relatively good knowledge base for developing programs to improve fetal growth, these efforts may have only a marginal impact on neonatal and infant mortality in developed countries.⁵⁴

In contrast, very little is known about the risk factors for preterm birth. For preterm births in developed countries, the primary risks are: (1) cigarette smoking; (2) prior preterm birth and spontaneous abortion; (3) low prepregnancy weight; and (4) *in utero* exposure to diethylstilbestrol (DES), a miscarriage deterrent used primarily in the 1950s in the United States.⁵²⁻⁵⁴ More than two-thirds of preterm deliveries could not be explained by known risk factors, and the proportion of preterm births attributed in this analysis to modifiable risk factors—that is, to smoking, low prepregnancy weight, and DES—was approximately 25%. (It should be noted that, while DES was identified as a

The most likely known targets for prenatal interventions to prevent low birth weight rates are (1) smoking, (2) nutrition, and (3) medical care.

contributor to low birth weight, its continued impact on birth weight may be time-limited. Its mention serves as a reminder that well-intended prenatal treatments can inadvertently or indirectly increase the risk of delivering a low birth weight infant.)

These results indicate that the most likely known targets for prenatal interventions to prevent low birth weight rates are (1) smoking (aimed at reduction or cessation); (2) nutrition (aimed at increas-

ing prepregnancy weight and/or ensuring adequate weight gain during pregnancy); and (3) medical care (aimed at reducing overall morbidity).⁵²⁻⁵⁴ These data also emphasize that an appreciable proportion of low birth weight deliveries in developed countries is due to unknown causes or is related to factors that cannot be modified during pregnancy. Some of these factors, for example, ethnicity, may be indicative of the long-term influence of adverse socioeconomic conditions which may be difficult to overcome with prenatal care.

Lowering Individual Risks

Although we do not know the primary causes for low birth weight and preterm birth, we do know at least three important steps that can be taken to reduce the rate

have ranged from 9% to 27%, and reduction rates, from 17% to 28%.⁵⁹⁻⁶¹

Smoking cessation methods are found to be modestly effective at getting women to stop or reduce smoking, except where interventions merely involve routine advice or when advice was not given to all smokers.^{62,63} Reduced smoking, as confirmed by biochemical tests during pregnancy, has been associated with improved mean birth weight in a number of intervention trials.^{57,58,64-66} However, most studies of interventions to stop smoking during pregnancy have been too small to detect differences in low birth weight or infant mortality rates. Many clinicians are not thoroughly trained in, nor do they have the time to provide, individualized smoking cessation counseling or reinforcement. Haddow and colleagues found that there was a 30% reduction in low birth weight in pregnancies managed by physicians who had the highest rates of completing the study's smoking cessation intervention.⁶⁴ There was little impact on those managed by physicians with lower rates of completing the intervention.⁶⁴

Clinical trials of smoking cessation interventions have reported significant effects on increasing birth weight.

of low birth weight. A short discussion of these factors is presented below. (For a more detailed discussion of individual lifestyle factors, see the article by Chomitz in this journal issue.)

Smoking Cessation

Smoking is a major preventable risk factor for low birth weight.⁵ In the wake of growing acceptance of the evidence linking smoking to adverse health effects, smoking is declining among women, although not as fast as among men. Some women report that they cease smoking on their own when they become pregnant (18% to 20%), and others reduce the amount they smoke (27% to 36%). However, about 25% of women who are pregnant continue to smoke throughout their pregnancy.⁵⁵ It has been estimated that as much as one-quarter of low weight births could be prevented if smoking during pregnancy were eliminated.⁵⁶

Some clinical trials of smoking cessation interventions have reported significant effects on increasing birth weight.^{57,58} Smoking cessation methods during pregnancy generally include health education, self-help techniques, or counseling programs. Some include home visits, and the more recent approaches include feedback to the woman of her own serum nicotine metabolites. Quit rates during pregnancy

Women who find the risks of smoking acceptable are least likely to quit.⁶⁷ Some women refer to their previous positive birth outcomes to refute the risks of smoking for them. Others, when trying to quit smoking, point out the unhealthy effects that their coping behaviors have on themselves and others.⁶⁸ In a group of British women who had given birth to low birth weight babies, 38% believed smoking was a cause of low birth weight, but only 10% thought smoking had anything to do with the fact that they had a low weight baby.⁶⁹ Overcoming the factors that lead to these beliefs is a challenge to prenatal care providers.

There is much to be done to disseminate smoking cessation programs within prenatal care.^{61,70} Given the substantial proportions of women who continue to smoke during pregnancy or relapse after stopping, developing and disseminating effective cessation programs that are practical for prenatal care settings offers one potentially fruitful approach to address this preventable precursor to low birth weight. In view of recent findings that the infants of mothers with passive smoke exposure during pregnancy are also at risk, efforts to modify smoking habits of family members of pregnant women may be further indicated.⁷¹

Nutritional Care

While there is substantial evidence associating low maternal weight gain and low prepregnancy weight with low birth weight,^{72–74} research studies do not clearly indicate that prenatal nutritional interventions will reliably prevent low birth weight deliveries. Randomized trials of supplementation have not found any particular supplement associated with reliable and appreciable improvements in birth weight.⁷⁴ The equivocal research findings regarding the impact of supplementation on birth weight in adequately nourished populations make it difficult to assume that assessment and counseling efforts alone will be highly associated with birth weight improvements.⁷⁴ Overall, the available research on the influence of nutrient supplementation of pregnant women on improved birth weight suggests that benefits may be largely limited to women who are chronically undernourished.⁷⁵

Medical Care

Although a specific medical condition may have a large individual effect on birth weight, most medical conditions affect only a small proportion of pregnant women and, therefore, may contribute little to overall low birth weight rates.^{5,76} Infections, sexually transmitted diseases, maternal hematological status, diabetes, and hypertension-related complications all heighten the risk of low weight births.⁵ While high-risk medical care in general, rather than specific medical interventions for specified conditions, might have a measurable impact on low weight births, not all medical interventions reduce the chances of low birth weight. High-risk, acute care to reduce IUGR or lower chances of preterm birth are limited in application and effect. Indeed, under specific conditions—for example, uncontrolled diabetes or severe hypertension—the appropriate intervention may be to induce labor and delivery even though doing so may increase the risk of a low weight birth.

Interventions to minimize the risks of intrauterine growth retardation must give specific attention to fetal growth. A Public Health Expert Panel recommended that maternal risk factors for impaired fetal growth be identified during prenatal screening.⁷² These factors include maternal hypertension, renal disease, heart disease, third trimester bleeding, multiple pregnancy, and sickle cell disease. In the presence of such risk factors and an abnormally low fundal height (abdominal meas-

urement of the mother) for a reliably determined gestational age, an ultrasound examination of the fetus, placenta, and amniotic fluid and monitoring of fetal well-being can aid in the management of a pregnancy for optimal fetal growth. There is little evidence that early delivery improves outcome, except for prevention of fetal death.⁷²

It is important to acknowledge that certain risks of low birth weight may be immutable once a woman is pregnant and has decided not to terminate the pregnancy. At the individual level, the effect of demographic risk factors on birth weight tends to be smaller than medical condition effects. Nevertheless, demographic risks affect larger numbers of women and may be more difficult to alter or ameliorate.⁷⁶ For example, limitations in the size and weight of newborns associated with the mother's or father's size (underweight and short) or the mother's birth weight are not likely to be reversible or may reflect natural variation that is unrelated to mortality. However, the higher rates of very low birth weight among teenage mothers and

Most medical conditions affect only a small proportion of pregnant women and, therefore, may contribute little to overall low birth weight rates.

black mothers may indicate that some demographic risk factors are partly amendable by population-based comprehensive preconception and prenatal interventions. The following discussion concentrates on the role of prenatal care in reducing low birth weight rates by implementing effective features of comprehensive care in populations rather than on a case-by-case basis.

Lowering Population Risks

Improving the nation's low birth weight rates will require more than simply improving the content of prenatal care and changing individual risk factors. System level approaches to impact the accessibility and appropriateness of delivery of health care services to entire groups of women with specifically identified characteristics associated with preventable risks of low birth weight also may be needed. Although observational studies often accompany

population-based interventions, there is a paucity of information from more rigorously designed evaluations to assess the impact of these innovations. A number of population-based interventions aimed at motivating and enabling women to optimize their health behaviors and maximize the benefits they might draw from health care services like prenatal care have been developed. Although the available evidence to support their efficacy is equivocal, they are areas for further investigation.

Improving the Use of Prenatal Care

Much attention has been given to the possibility that, in the absence of randomized trials of prenatal care, the observed association between adequate prenatal care utilization and lower rates of low weight births may, in part, reflect the individual and social characteristics of women who choose to use prenatal care early and

In a national study of low-income women, 71 % of the women experienced a problem getting prenatal care.

often. Thus, an important area for continuing inquiry is the exploration of what maternal, paternal, and social factors contribute to the adequate use of prenatal care. Interventions that improve compliance with advice to obtain prenatal care early and continuously throughout pregnancy may be found to improve compliance with other advice given during prenatal care visits, for example, to stop smoking. It has already been reported that belief in the benefits of prevention in general and prenatal care specifically is associated with adequate care use.^{77,78} In addition, women who receive adequate prenatal care are also more likely to get preventive care for their infants.⁷⁸

Women who get inadequate amounts of prenatal care do so for a variety of reasons related to characteristics of the health care system, provider practices, and their own individual and social characteristics.⁷⁹ Numerous financial, cultural, and system barriers to prenatal care access have been identified.⁷⁹ In a national study of low-income women, 71% of the women experienced a problem getting prenatal care and, on average, indicated three distinct barriers.⁸⁰ Those who received the least prenatal care cited finances as the

“most important reason” for not getting prenatal care sooner or more often. However, as these women were more likely to cite multiple access problems, improving prenatal care access and use may require more than overcoming health care system financial barriers. Women next cited transportation and child care as additional barriers to prenatal care access.

Motivating positive attitudes toward pregnancy is important.⁸¹ Women whose pregnancy is unwanted, who have negative attitudes about being pregnant, or who unintentionally became pregnant are more likely to delay prenatal care or to miss appointments.^{82,83} Women who obtain late or no prenatal care are more likely to have considered abortion than adequate prenatal care users.⁸⁴ A recent study found that, prior to the availability of abortion, women who indicated that they or their husbands were unhappy, resentful, or upset about the pregnancy, who did not want the pregnancy, or who had a mistimed pregnancy were more than twice as likely to have a neonatal death, though not a low birth weight baby.⁸⁵ Denial and depression have also been associated with poor use of prenatal care, especially among adolescents.⁸⁶ The woman's partner and family social support network have also been found to be associated with use of adequate care, though findings conflict because of differing definitions of social support and differences in the populations studied.⁸⁷ Women living with the father or a sexual partner were more likely to receive adequate prenatal care visits than women living with adult relatives.⁸⁸ However, conflict or problems with the father of the baby have been found to act as deterrents to early and continuous prenatal care use.^{89,90} Familial support and discussions of pregnancy and prenatal care have been shown to have only modest or no measurable effects on a woman's actual use of care.^{77,86,91}

Patient satisfaction with health care in general is a current aim of quality assurance efforts in the United States.⁹² What is most important to pregnant women in their care has only recently been studied. Women who are satisfied with their care and view their physicians as competent and concerned about their welfare are more likely to receive adequate amounts of care.⁸⁴ On the other hand, negative attitudes toward health care and health care providers may lead women to reject

the importance of prenatal care and seek care less often.

Women who disagree with their physicians regarding health risks are less likely to get care.⁹³ Having a baby too soon or too small is of concern to most women, but their own perceptions of when is too soon, what is too small, and what is a problem vary. A small baby in and of itself is not considered a risk by women in general. When asked, many women will respond that a smaller baby is easier in labor and delivery. A British study of pregnant women who had previously had a low birth weight baby—one of the few studies to look at women's views of the risks of low birth weight—found that more than a third of women (37%) did not see low birth weight as a problem.⁶⁹ Yet 63% of these women said that the baby had been in an intensive care unit, and 72% said that the child had problems after birth. Some 15% said they did not think the child was developing normally and 42% said they had continuing worries about the child's development.

Clearly, the determinants of prenatal care use are varied and range from obvious financial, geographic, and support barriers to more subtle cultural and attitudinal characteristics. Through the expansion of Medicaid eligibility, nationwide efforts to reduce the financial barriers to prenatal care access have been under way for some years.⁹⁴ Preliminary reports indicate that these efforts have increased prenatal care use.^{95,96} These reports are encouraging given the established benefits that prenatal care can provide in the areas of maternal morbidity and mortality and the potential to encourage subsequent health care utilization.⁷⁸ Nevertheless, between 1981 and 1991, the incidence of low birth weight in the United States increased.⁹⁷ Further, the proportion of women getting no care or starting prenatal care in the third trimester also increased.⁹⁷

To the extent that managed care plans under Medicaid will increasingly become the usual source of care for low-income pregnant women, some of the current providers of enhanced perinatal services may be displaced. Publicly funded agencies, maternal and infant care projects, and health departments, typically seen as having the capacity and experience to provide the ancillary services that enhance the comprehensiveness of prenatal care, have traditionally provided prenatal care services to segments of the population at

higher risk. The maintenance or transfer of this capacity and experience under managed care or a health care reform scenario is a matter for policy attention.

Providing Preconception Care

Continuous access to health care, not only early in pregnancy but also before and after pregnancy, has been advocated as a means to improve health outcomes of pregnancy, although there is a paucity of rigorous evidence to establish the potential impact of this proposal. Availability of abortion services and, to a lesser extent, family planning services has been associ-

Continuous access to health care, not only early in pregnancy but also before and after pregnancy, has been advocated as a means to improve health outcomes of pregnancy.

ated with lower rates of low weight births.^{98,99} In addition, preconception care is currently practiced in some places as a part of maternal and fetal medical care, family planning, and ongoing primary care.¹⁰⁰ Many low birth weight risks predate a woman's pregnancy, and specific interventions exist to reduce prepregnancy risks such as smoking, alcohol and drug use, inadequate weight for height, poor nutritional status, and chronic or recurrent diseases, including sexually transmitted diseases, reproductive tract infections, hypertension, and diabetes.^{5,73} Women should be immune to rubella before pregnancy. Although outbreaks of rubella are relatively rare, congenital rubella syndrome effects on fetuses can be devastating in early stages of pregnancy. Women should also be queried about the need for genetic counseling prior to becoming pregnant.

The role of preconception care in improving pregnancy outcomes in general and low birth weight rates in particular remains a topic for investigation. There are well-established methods for determining the relative value of screening tests and treatment in women of varying risks. It is important to assess the individual and cumulative benefit to prepregnancy screening and treatment for conditions with high risk of low birth weight.

Delivering Specialized Prenatal Care

Teenage pregnancy programs serve a population group at distinct high risk of low weight births and are generally a mix of health care, education, and social services in coordination with local agencies. Core services include prenatal, postpartum, and pediatric health care, remedial education, employment training and counseling, family planning services, life

A vital area for reducing low birth weight rates may lie with improving socioeconomic conditions.

planning assistance and life skills training, and parenting education. In addition, many comprehensive care programs have featured a case management approach in which individualized service plans are developed on the basis of individual needs assessments.¹⁰¹ The programs are usually based in schools, health facilities, or the teens' homes. Besides providing psychosocial, nutritional, medical, and health education services, these programs also offer parenting education, encourage continued schooling, urge adolescents to delay subsequent pregnancies, prepare them for employment, and assist them with legal, family, and financial problems. In nonrandomized studies, some of these programs

have been found to be associated with higher-than-expected birth weights.²⁹

Prenatal home visiting programs are designed to take aspects of prenatal care into the homes of women who live in high-risk communities. The use of both nurses and lay health workers as home visitors has been revived in recent years as attention has been paid to psychosocial and environmental risk factors for low weight births of the socially disadvantaged. Home visiting is routine in many European countries, where it is usually conducted by midwives. However, many recent pilot projects in this country have used lay health workers from the community. While this intervention has attracted considerable attention as a potentially viable approach to improving birth weights, the evidence regarding its effectiveness remains open to debate.^{8,10,102}

Involving Cultures and Communities in Developing Prenatal Care

A vital area for reducing low birth weight rates may lie with improving socioeconomic conditions. Improvement in low birth weight rates might be expected if the health, well-being, resources, and prenatal care of the advantaged women in this country could be more widely distributed and if improvements in education, employment, and child care opportunities could be achieved.⁵ Focusing culturally competent outreach and prenatal care efforts in disadvantaged communities may also be a potentially viable area for the improvement of low birth weight rates.⁷⁹

Cultural and community-based enhancements of prenatal care have not been evaluated for their impact on low weight births.

Community empowerment is a process of enabling groups to develop the authority to act, control, or influence consequences that are important to their members. Since the beginnings of the development of prenatal care, it has been recognized that community conditions such as poverty and racism can create circumstances in people's lives that heighten the risks of morbidity, mortality, and the inadequate use of preventive resources.¹⁰³ Empowerment is improving the distribution of the political resources conducive to health and well-being. The concept of empowerment of neighborhoods has led to a recent revival of the ideas of community health workers and community health centers, whose broader role is seen as family life community centers. The notion of empowerment has become entwined with the activities of the culturally focused movements to promote family conditions and parental competencies and behaviors that contribute to maternal and infant health and development.^{104,105}

The persistent lower rates of low weight births in certain cultural groups, even after adjustments for known differences in risk factors among these groups, have raised concerns that prenatal care should be adapted to specific cultures to be most effective. Culturally sensitive services are those in which there is an appreciation or admiration for the cultural characteristics of a group, and culturally competent services refer to those that accept, respect, and give attention to cultural differences in knowledge, values, beliefs, and customs.^{106,107} At the programmatic level, it is recognized that realignments of agency efforts are needed to collaborate with communities in the joint development of goals and directions and to share responsibility for goals, resource development, risks, and rewards.¹⁰⁸

Conclusions

In 1932, Dr. F. Browne observed that "much of what passes under the guise of antenatal care is too irregular, too infrequent, too ill-organized and perfunctory to deserve the name and it can never accomplish anything . . ."¹⁰⁹ There have been many improvements in prenatal care since then. Nevertheless, the most recent com-

prehensive review of the content of prenatal care concluded that, "to continue the process of refining the content of prenatal care to meet the objectives for pregnant woman, the infant, and the family, changes in public policy and prenatal care provider delivery of health care services must take place."⁷²

While lack of prenatal care has been highly associated with low birth weight in numerous studies, this relationship has been difficult to understand from a medical point of view as it has been observed that there is little done during the standard prenatal care visit that could be expected to reduce low birth weight.¹¹⁰ A more detailed examination of the available evidence and its limitations suggests that the potential direct impact of prenatal care on low birth weight may be far less than popularly assumed. On an individual level, there are three specific areas—for example, smoking cessation, nutrition of the malnourished, and medical care—where prenatal care can have an impact, particularly in reducing the number of small-for-gestational-age infants. Populationwide health promotion, social service, and case management approaches may of-

There is little done during the standard prenatal care visit that could be expected to reduce low birth weight.

fer further potential benefits, but data to link the provision of these services to reductions in low birth weight are lacking.

The very language of much of the research on the impact of prenatal care reflects a predisposition toward viewing prenatal care as a medical procedure to be doled out in units of service (the visit) or types of service. The use of visits as the measure of care is a natural extension of this point of view, which de-emphasizes the role of the mother, father, family, and the community in fostering a social and physical environment that enhances a positive pregnancy process. When an impression is created that prenatal care is a specific health care intervention that can be injected on a case-by-case basis to reduce low birth weight and other adverse pregnancy outcomes, populationwide and community-focused approaches may be overlooked. The ultimate success of pre-

natal care in reducing current low birth weight percentages in the United States may hinge on the development of a much broader and more unified conception of prenatal care than currently prevails. It has yet to be explored if interventions focused on building cohesive, functional commu-

The ultimate success of prenatal care in reducing current low birth weight percentages in the United States may hinge on the development of a much broader and more unified conception of prenatal care than currently prevails.

nities can do as much or more to provide women effective social support and a caring, safe environment.

Numerous attempts have been made to estimate the cost-effectiveness of prenatal care services.^{5,111} For each dollar spent on prenatal care, expected medical cost savings have been estimated to range from \$2.57 to \$3.38.^{5,111} However, these estimates of the cost-effectiveness of prenatal care may be overstated given the unquantified differences in women who do and do not use prenatal care and the equivocal effectiveness of preterm prevention programs. Nevertheless, the long-term effects of comprehensive prenatal care on improving healthful behaviors and increasing use of preventive health care for infants and potentially all members of the family may be understated.⁷⁸ While considerable policy discourse has focused on the association of prenatal care with low birth weight, the benefits of prenatal care for maternal, infant, and family health should not be overlooked. To the extent that the value of prenatal care is narrowly viewed and promoted mainly in terms of its impact on low birth weight, its much broader impact and importance may be ignored.

Recommendations

So what can be done and by whom to maximize the impact of prenatal care on low birth weight and other adverse pregnancy outcomes? The following list offers some suggestions to the major groups involved.

To the Biomedical Community

1. Continue the current practice of screening for and treating disease conditions that complicate pregnancies and increase the risk of poor outcomes.

2. Pursue efforts to investigate and assure the public of the effectiveness and appropriate timing of services provided. Tradition and provider convenience should not obscure the importance of demonstrating efficacy and encouraging the active involvement of both mother and family in the pregnancy process.

3. Expand efforts to screen for and treat nonmedical risk-related conditions, including substance abuse, physical abuse, nutritional deficiencies, concrete living need deficiencies, infant and child care educational needs, and the like. In total, prenatal care offers the opportunity to undertake a comprehensive needs assessment that has relevance not only to the current pregnancy, but also to the future health of the mother, the infant, the family, and the children to follow.

4. Based on this assessment, provide appropriate linkages with public health and social services institutions to assure comprehensiveness of care and needed ancillary services, that is, make and follow-up on referrals.

5. Improve the content of prenatal care in terms of advice about health behaviors. Too many women are not getting the full range of recommended advice on such important topics as breast feeding and substance use cessation.^{15,34}

6. Develop and promote the culturally competent practice of prenatal care.

7. As the establishment of a positive pattern of health care utilization during pregnancy may further promote the positive future use of preventive health care, including prenatal care, for the mother, infant, and family members, establish partnerships with public health and other agencies to facilitate and assure adequate continuation of prenatal care once it has been begun.

To the Public Health Community

1. Promote a systems integration approach to prenatal care that enables linkages with the medical community for follow-up, case management, and ancillary services and assures continuity of coordinated, risk-appropriate care.

2. Provide populationwide (not just high-risk) preconception and prenatal education to encourage family planning, reproductive health, and health promotion. Give all women the information they need to play a lead role in assuring their reproductive health.

3. Undertake outreach and follow-up efforts.

4. Continue to monitor and assess health status outcomes, document risk indicators, and evaluate interventions for all women and infants.

5. Provide leadership toward the development of community involvement and empowerment in perinatal issues.

6. Advocate policies that facilitate access to and availability of services.

7. Advocate and undertake interventions to reduce stressors related to disparate socioeconomic conditions.

To the Public and Our Communities

1. Encourage and support every woman's active involvement in decision making and care.

2. Encourage populationwide approaches that increase community involvement.

3. Encourage cultural competence on the part of providers to increase acceptability.

4. Advocate and politically support efforts to assure affordable and accessible prenatal care to all so that our children will have the best possible start in life.

To the Research Community

1. Direct research efforts on the effectiveness of the content of prenatal care, including preconception care and the nutritional and psychosocial aspects of care.^{5,72}

2. Focus research efforts on the impact of the individual components of prenatal care and their use in combinations.⁵

3. Expand research efforts on the impact of prenatal care beyond measures of birth weight and preterm delivery. Look, for example, at maternal health, child health, and subsequent health care utilization.

4. Develop improved strategies to measure the adequacy of prenatal care utilization and to assess the content and quality of prenatal care.

5. Focus research on improving the measurement of gestational age in populations in an effort to facilitate preterm

birth prevention research. In spite of the reliability of the birth weight measure, it is now widely recognized that prevention and evaluation efforts should be more specifically focused on the determinants of preterm and very preterm delivery, not on low birth weight.⁵²

6. Place emphasis on the use of randomized controlled trials for assessing the efficacy of prenatal care interventions.

7. Support efforts to review and assess current prenatal care practice standards.

Reform of the health care system offers an opportunity to shape a future that promotes the health of infants and women, facilitates reproductive choice, and assures access and availability of comprehensive health care and ancillary services—all of which are needed to reduce the risks of low birth weight. However, we must undertake these efforts with the recognition that, while adequate, comprehensive prenatal care is a necessary and important part of the solution, it may not be sufficient to effect the dramatic reduction in low birth weight in the United States that many have anticipated. The current evidence and collective experience regarding the role of prenatal care in the prevention of low birth weight remains mixed and does not support an unequivocal assumption that universal access to prenatal care as presently perceived will either result in

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major declines in low birth weight percentages or markedly reduce the current disparities among population subgroups. We must prepare now for the difficult task of reeducating policymakers and the public regarding the value of prenatal care and the importance of universal access without using the prevention of low birth weight as the primary argument. In addition, other avenues to reduce low birth weight and preterm delivery must be explored.

1. Taussig, F.J. The story of prenatal care. *American Journal of Obstetrics and Gynecology* (1937) 34,5:731–39.
2. Thompson, J.E., Walsh, L.V., and Merkatz, I.R. The history of prenatal care: Cultural, social, and medical contexts. In *New perspectives on prenatal care*. I.R. Merkatz and J.E. Thompson, eds. New York: Elsevier, 1990, pp. 9–30.
3. Speert, H. Prenatal care. In *Obstetrics and gynecology in America: A history*. Chicago: American College of Obstetrics and Gynecology, 1980, pp. 142–45.
4. Rosenberg, K., and Twaddle, S. Screening and surveillance of pregnancy hypertension—An economic approach to the use of day care. *Baillière's Clinical Obstetrics and Gynecology* (March 1990) 4,1:89–107.
5. Institute of Medicine, Committee to Study the Prevention of Low Birth Weight. *Preventing low birthweight*. Washington, DC: National Academy Press, 1985.
6. Hughley, M.J. Routine prenatal and gynecologic care in prepaid group practice. *Journal of the American Medical Association* (1986) 256,13:1775–77.
7. Terris, M., and Glasser, M. A life table analysis of the relation of prenatal care to prematurity. *American Journal of Public Health* (1974) 64,9:869–75.
8. Alexander, G.R., Weiss, J., Hulsey, T.C., and Papiernik, E. Preterm birth prevention: An evaluation of programs in the United States. *Birth* (1991) 18,3:160–69.
9. Main, D., Gabble, S.G., Richardson, D., and Strong, S. Can preterm deliveries be prevented? *American Journal of Obstetrics and Gynecology* (1985) 151,7:892–96.
10. Heins, H.C., Nance, N.W., McCarthy, B.J., and Efird, C.M. A randomized trial of nurse-midwifery prenatal care to reduce low birth weight. *Obstetrics and Gynecology* (1990) 75,3:341–45.
11. Collaborative Perinatal Group. Multi-center randomized, controlled trial of preterm birth prevention program. *American Journal of Obstetrics and Gynecology* (1993) 169:352–66.
12. Olds, D.L., Henderson, C.R., Tatelbaum, R., and Chamberlin, R. Improving the delivery of prenatal care and outcomes of pregnancy: A randomized trial of nurse home visitation. *Pediatrics* (1986) 77,1:16–28.
13. Spencer, B., Thomas, H., and Morris, J. A randomized controlled trial of the provision of a social support service during pregnancy: The South Manchester Family Worker Project. *British Journal of Obstetrics and Gynaecology* (1989) 96:281–88.
14. McLaughlin, F.J., Altemeier, W.A., Christensen, M.J., et al. Randomized trial of comprehensive prenatal care for low-income women: Effect on infant birth weight. *Pediatrics* (1992) 89,1:128–32.
15. Villar, J., Farnot, U., Barros, F., et al. A randomized trial of psychosocial support during high-risk pregnancies. *New England Journal of Medicine* (1992) 327,18:1266–71.
16. Hobel, C.J., Ross, M.G., Bemis, R.L., et al. The West Los Angeles Preterm Birth Prevention Project. I. Program impact on high-risk women. *American Journal of Obstetrics and Gynecology* (January 1994) 170:54–62.
17. Strobino, D.M., Chase, G.A., Kim, Y.J., et al. The impact of the Mississippi Improved Child Health Project on prenatal care and low birth weight. *American Journal of Public Health* (1986) 76,3:274–78.
18. Sokol, R.J., Woolf, R.B., Rosen, M.G., and Weingarden, K. Risk, antepartum care and outcome: Impact of a maternity and infant care project. *Obstetrics and Gynecology* (1980) 56:150–56.
19. Peoples, M.D., and Siegel, E. Measuring the impact of programs for mothers and infants on prenatal care and low birth weight: The value of refined analysis. *Medical Care* (1983) 21,6:586–608.
20. Peoples, M.D., Grimson, R.C., and Daughtry, G.L. Evaluation of the effects of the North Carolina Improved Pregnancy Outcome Project: Implications for state-level decision-making. *American Journal of Public Health* (1984) 74,6:549–54.
21. Buescher, P.A., Smith, C., Holliday, J.L., and Levine, R.H. Source of prenatal care and infant birth weight: The case of a North Carolina county. *American Journal of Obstetrics and Gynecology* (1987) 156,1:204–10.
22. Korenbrot, C.C. Risk reduction in pregnancies of low income women: Comprehensive prenatal care through the OB Access Project. *Mobius* (1984) 4,3:34–43.
23. Shadish, W.R., and Reis, J. A review of studies of the effectiveness of programs to improve pregnancy outcomes. *Evaluation Review* (1984) 8:747–76.

24. Cartoof, V.G., Klerman, L.V., and Zazueta, V.D. The effect of source of prenatal care on care-seeking behavior and pregnancy outcomes among adolescents. *Journal of Adolescent Health* (1991) 12,2:124–29.
25. Petitti, D.B., Hiatt, R.A., Chin, V., and Croughan-Minihane, M. An outcome evaluation of the content and quality of prenatal care. *Birth* (1991) 18,1:21–25.
26. Buescher, P.A., and Ward, N.I. A comparison of low birth weight among Medicaid patients of public health departments and other providers of prenatal care in North Carolina and Kentucky. *Public Health Report* (1992) 107,1:54–59.
27. Devaney, B., Bilheimer, L., and Schore, J. Medicaid costs and birth outcomes: The effects of prenatal WIC participation and the use of prenatal care. *Journal of Policy Analysis and Management* (1992) 11,4:573–92.
28. Handler, A., and Rosenberg, D. Improving pregnancy outcomes: Public versus private care for urban, low-income women. *Birth* (1992) 19,3:123–30.
29. Korenbrot, C.C., Showstack, J., Loomis, A., and Brindis, C. Birth weight outcomes in a teenage pregnancy case management project. *Journal of Adolescent Health Care* (1989) 10:97–104.
30. Lennie, J.A., Klun, J.R., and Hausner, T. Low birth weight rate reduced by the obstetrical access project. *Health Care Financing Review* (1987) 8,3:83–86.
31. Kogan, M.D., Alexander, G.R., Kotelchuck, M., and Nagey, D. Relation of the content of prenatal care to the risk of low birth weight. *Journal of the American Medical Association* (1994) 271,17:1340–45.
32. Freda, M.C., Andersen, H.F., Damus, K., and Merkatz, I.R. Are there differences in information given to private and public prenatal patients? *American Journal of Obstetrics and Gynecology* (1993) 169:155–60.
33. Hansell, M.J. Sociodemographic factors and the quality of prenatal care. *American Journal of Public Health* (1991) 81,8:1023–28.
34. Brett, K.M., Schoendorf, K.C., and Kiely, J.L. Differences between black and white women in the use of prenatal care technologies. *American Journal of Obstetrics and Gynecology* (1994) 170:41–46.
35. Kogan, M.D., Kotelchuck, M., Alexander, G.R., and Johnson, W.E. Racial disparities in reported prenatal care advice from health care providers. *American Journal of Public Health* (1994) 84,1:82–88.
36. Kogan, M.D., Alexander, G.A., Kotelchuck, M., et al. Comparing mothers' reports on the content of prenatal care received with recommended national guidelines for care. *Public Health Reports* (September/October 1994) 109,5:637–46.
37. Eastman, N.J. Prematurity from the viewpoint of the obstetrician. *American Practitioner* (1947) 1,7:343–52.
38. Yankauer, A., Goss, K.G., and Romeo, S.M. An evaluation of prenatal care and its relationship to social class and social disorganization. *American Journal of Public Health* (1953) 43:1001–10.
39. Baumgartner, L., Gold, E.M., Jacobziner, H., et al. Prenatal care in New York City, 1951. *Public Health Reports* (1954) 69,10:937–44.
40. Rosenfeld, L.S., and Donabedian, A. Prenatal care in metropolitan Boston. *American Journal of Public Health* (1958) 48,9:1115–24.
41. Donabedian, A., and Rosenfeld, L.S. Some factors influencing prenatal care. *New England Journal of Medicine* (1961) 265,1:1–6.
42. Shwartz, S. Prenatal care, prematurity, and neonatal mortality. *American Journal of Obstetrics and Gynecology* (1962) 83,5:591–98.
43. Harris, J.E. Prenatal medical care and infant mortality. In *Economic aspects of health*. V. Fuchs, ed. Chicago: University of Chicago Press, 1982, pp. 15–52.
44. Alexander, G.R., Tompkins, M.E., Petersen, D.J., and Weiss, J. Sources of bias in prenatal care utilization indices: Implications for evaluating the Medicaid expansion. *American Journal of Public Health* (1991) 81,8:1013–16.
45. Kessner, D.M., Singer, J., Kalk, C.E., and Schlesinger, E.R. *Infant death: An analysis by maternal risk and health care*. Washington, DC: Institute of Medicine, 1973.
46. Alexander, G.R., and Cornely, D.A. Prenatal care utilization: Its measurement and relationship to pregnancy outcome. *American Journal of Preventive Medicine* (1987) 3,5:243–53.
47. Gortmaker, S.L. The effects of prenatal care upon the health of the newborn. *American Journal of Public Health* (1979) 69,7:653–60.

48. Kotelchuck, M. An evaluation of the Kessner Adequacy of Prenatal Care Index and a proposed adequacy of prenatal care utilization index. *American Journal of Public Health* (1994) 84,9:1414–20.
49. Tyson, J., Guzick, D., Rosenfeld, C.R., et al. Prenatal care evaluation and cohort analyses. *Pediatrics* (1990) 85,2:195–204.
50. Malloy, M.H., Kao, T., and Lee, Y.J. Analyzing the effect of prenatal care on pregnancy outcome: A conditional approach. *American Journal of Public Health* (1992) 82,3:448–50.
51. National Center for Health Statistics. (1991). *Linked birth and infant death data set: 1986 birth cohort*. [Data tape.] Available: Mortality Statistics Branch, Division of Vital Statistics, NCHS, Centers for Disease Control and Prevention, 6525 Belcrest Rd., Rm. 840, Hyattsville, MD 20782, (301) 436-8884.
52. Kramer, M.S. Determinants of low birth weight: Methodological assessment and meta-analysis. *Bulletin of the World Health Organization* (1987) 65:663–737.
53. Kramer, M.S. Intrauterine growth and gestational duration determinants. *Pediatrics* (1987) 80,4:502–11.
54. Kramer, M.S. Birth weight and infant mortality: Perceptions and pitfalls. *Paediatric and Perinatal Epidemiology* (1990) 4:381–89.
55. Murata, P.J., McGlynn, E.A., Siu, A.L., and Brook, R.H. *Prenatal care: A literature review and quality assessment criteria*. Santa Monica, CA: RAND, 1992.
56. Kleinman, J., Mitchell, B., Madan, J.H., et al. The effects of maternal smoking on fetal and infant mortality. *American Journal of Epidemiology* (1988) 127,2:274–82.
57. Hebel, J.R., Fox, N.L., and Sexton, M. Dose-response of birth weight to various measures of maternal smoking during pregnancy. *Journal of Clinical Epidemiology* (1988) 41:483–89.
58. Sexton, M., and Hebel, J.R. A clinical trial of change in maternal smoking and its effect on birth weight. *Journal of the American Medical Association* (1984) 251:911–15.
59. Ershoff, D., Quinn, V.P., Mullen, P.D., and Lairson, D.R. Pregnancy and medical cost outcomes of a self-help prenatal smoking cessation program in an HMO. *Public Health Reports* (1990) 105:340–47.
60. MacArthur, C., Newton, J.R., and Knox, E.G. Effect of anti-smoking health education on infant size at birth: A randomized controlled trial. *British Journal of Obstetrics and Gynaecology* (1987) 94:295–300.
61. Windsor, R.A., Lowe, J.B., Perkins, L.L., et al. Health education for pregnant smokers: Its behavioral impact and cost benefit. *American Journal of Public Health* (1993) 83:201–6.
62. Windsor, R.A., Li, C.Q., Lowe, J.B., and Goldenberg, R.L. Evaluation of the impact of dissemination of smoking cessation methods on the low birthweight rate and health care costs: Achieving Year 2000 objectives for the nation. *American Journal of Preventive Medicine* (1992) 8,3:171–77.
63. Mullen, P.D. Smoking cessation counseling in prenatal care. In *New perspectives on prenatal care*. I.R. Merkatz and J.E. Thompson, eds. New York: Elsevier, 1990, pp. 161–76.
64. Haddow, J.E., Knight, G.J., Kloza, E.M., et al. Cotinine-assisted intervention in pregnancy to reduce smoking and low birthweight delivery. *British Journal of Obstetrics and Gynaecology* (1991) 98:859–65.
65. Li, C.Q., Windsor, R.A., Perkins, L., et al. The impact on infant birth weight and gestational age of cotinine-validated smoking reduction during pregnancy. *Journal of the American Medical Association* (1993) 269,12:1519–24.
66. Rush, D., Orme, J., King, J., et al. A trial of health education aimed to reduce cigarette smoking among pregnant women. *Paediatric and Perinatal Epidemiology* (1992) 6,2:285–97.
67. O'Connor, A., Davies, B.L., Dulberg, C.S., et al. Psychometric properties of health risk attitude measures in predicting cessation among pregnant smokers. *Medical Care* (1993) 31,7:658–62.
68. Baric, J., MacArthur, C., and Sherwood, M. A study of health education aspects of smoking in pregnancy. *International Journal of Health Education* (1976) 19,2:1–17.
69. Rajan, L., and Oakley, A. Low birth weight babies: The mother's point of view. *Midwifery* (1990) 6:73–85.
70. Floyd, R.L., Sahniser, C., Gunter, E.P., and Kendrick, J.S. Smoking during pregnancy, prevalence, effects and intervention strategies. *Birth* (1991) 18,1:48–53.
71. Eliopoulos, C., Klein, J., Phan, M.K., et al. Hair concentrations of nicotine and cotine in women and their newborn infants. *Journal of the American Medical Association* (1994) 271,8:621–23.

72. *Caring for our future: The content of prenatal care.* A report of the Public Health Service Expert Panel on the Content of Prenatal Care. Washington, DC: U.S. Department of Health and Human Services, 1989.
73. Worthington-Roberts, B., and Klerman, L.V. Maternal nutrition. In *New perspectives on prenatal care.* I.R. Merkatz and J.E. Thompson, eds. New York: Elsevier, 1990, pp. 235–71.
74. Institute of Medicine, Subcommittee on Nutritional Status and Weight Gain During Pregnancy. *Nutrition during pregnancy.* Washington, DC: National Academy Press, 1990.
75. Susser, M. Maternal weight gain, infant birth weight, and diet: Causal sequences. *American Journal of Clinical Nutrition* (1991) 53:1384–96.
76. Hulsey, T.C., Patrick, C.H., Alexander, G.R., and Ebeling, M. Prenatal care and prematurity: Is there an association in uncomplicated pregnancies? *Birth* (1991) 18,3:146–50.
77. Zweig, S., LeFevre, M., and Kruse, J. The health belief model and attendance for prenatal care. *Family Practice Research Journal* (1988) 8:32–34.
78. Butz, A.M., Funkhouser, A., Caleb, L., and Rosenstein, B.J. Infant health care utilization predicted by pattern of prenatal care. *Pediatrics* (1993) 92,1:50–54.
79. Institute of Medicine, Committee to Study Outreach of Prenatal Care. S. Brown, ed. *Prenatal care: Reaching mothers, reaching infants.* Washington, DC: National Academy Press, 1988.
80. U.S. General Accounting Office, Comptroller General of the United States. *Prenatal care: Medicaid recipients and uninsured women obtain insufficient care.* A report to the Congress of the United States. HRD-87-137. Washington, DC: GAO, September 1987.
81. Tiedje, L.B., Kingry, M.J., and Stommel, M. Patient attitudes concerning health behaviors during pregnancy: Initial development of a questionnaire. *Health Education Quarterly* (1992) 19:481–93.
82. Joseph, C.L.M. Identification associated with factors associated with delayed antenatal care. *Journal of the National Medical Association* (1989) 81:57–63.
83. Cooney, J.P. What determines the start of prenatal care? *Medical Care* (1985) 23,8:986–97.
84. Joyce, K., Diffenbacher, G., Greene, J., and Sorokin, Y. Internal and external barriers to obtaining prenatal care. *Social Work in Health Care* (1983) 9:89–96.
85. Bustan, M.N., and Coker, A.L. Maternal attitude toward pregnancy and the risk of neonatal death. *American Journal of Public Health* (1994) 84,6:513–19.
86. St. John, C., and Winston, T.J. The effect of social support on prenatal care. *Journal of Applied Behavioral Science* (1989) 25:79–98.
87. Augustyn, M., and Maiman, L.A. Psychological and sociological barriers to prenatal care. *Women's Health Issues* (1994) 4,1:20–28.
88. Casper, L.M., and Hogan, D.P. Family networks in prenatal and postnatal health. *Social Biology* (1990) 37:84–101.
89. Lia-Hoagberg, B., Rode, P., Skovholt, C.J., et al. Barriers and motivators to prenatal care among low-income women. *Social Science and Medicine* (1990) 30:487–95.
90. Young, C.L., McMahon, J.E., Bowman, V.M., and Thompson, D.S. Psychosocial concerns of women who delay prenatal care. *Families in Society* (1990) 71:408–15.
91. Moss, N.E., and Hensleigh, P.A. Initiation of prenatal care by adolescent: Associations with social support, stress, and Hispanic ethnicity. *Journal of Perinatology* (1989) 10:170–74.
92. Reiser, S.J. The era of the patient: Using the experience of illness in shaping the missions of health care. *Journal of the American Medical Association* (1993) 269:1012–17.
93. Simpson, H., and Walker, G. When do pregnant women attend for antenatal care? *British Medical Journal* (1980) 281:797–801.
94. Schlesinger, M., and Kronebusch, K. The failure of prenatal care policy for the poor. *Health Affairs* (Winter 1990) 9,4:91–111.
95. Piper, J.M., Ray, W.A., and Griffin, M.R. Effects of Medicaid eligibility expansion on prenatal care and pregnancy outcome in Tennessee. *Journal of the American Medical Association* (1990) 264,17:2219–23.
96. Haas, J.S., Udvarhelyi, S., Morris, C.N., and Epstein, A.M. The effect of providing coverage to poor uninsured pregnant women in Massachusetts. *Journal of the American Medical Association* (1993) 269,1:8791.
97. Centers for Disease Control and Prevention. Increasing incidence of low birth weight—United States, 1981–1991. *Morbidity and Mortality Weekly Report* (1994) 43,18:335–39.

98. Joyce, T.J., and Grossman, M. The dynamic relationship between low birthweight and induced abortion in New York City. An aggregate time-series analysis. *Journal of Home Economics* (1990) 9:273–88.
99. Jamieson, D.J., and Buescher, P.A. The effect of family planning participation on prenatal care use and low birth weight. *Family Planning Perspectives* (1992) 24,5:214–18.
100. Jack, B., and Culpepper, L. Preconception care. In *New perspectives on prenatal care*. I.R. Merkatz and J.E. Thompson, eds. New York: Elsevier, 1990, pp. 69–88.
101. Brindis, C.D., Barth, R.P., and Loomis, A.B. Continuous counseling: Case management with teenage parents. *Journal of Contemporary Social Work* (March 1987) :164–72.
102. Poland, M.L., Gilban, P.T., Waller, Jr., J.B., and Hankin, J. Effects of a home visiting program on prenatal care and birthweight: A case comparison study. *Journal of Community Health* (1992) 17,4:221–29.
103. Braithwaite, R.L., and Lythcott, N. Community empowerment as a strategy for health promotion for black and other minority populations. *Journal of the American Medical Association* (1989) 261,2:282–83.
104. Edelman, M.W. *Families in peril: An agenda for social change*. Cambridge, MA: Harvard University Press, 1987.
105. Weiss, H., and Halpern, R. *Community-based family support and education programs: Something old or something new?* New York: National Center for Children in Poverty, Columbia University, 1990.
106. Carrillo, J.E., and de la Cancela, V. The Cambridge Hospital Latino Health Clinic: A model for interagency integration of health services for Latinos at the provider level. *Journal of the National Medical Association* (1992) 84,6:513–19.
107. Rooda, L., and Fay, G. Staff development for culturally sensitive nursing care. *Journal of Nursing Staff Development* (1993) 9,6:262–65.
108. Andrews, K., and Urbain, E.S. *Interagency collaboration efforts to strengthen families*. St. Paul, MN: Amherst H. Wilder Foundation, 1991.
109. Browne, F.J. Antenatal care and maternal mortality. *Lancet* (1932) 5679:1–4.
110. Stubblefield, P.G. Causes and prevention of premature birth: An overview. In *Preterm birth: Causes, prevention, and management*. 2d ed. A. Fuchs, F. Fuchs, and P.G. Stubblefield, eds. New York: McGraw-Hill, 1993, pp. 3–39.
111. Gorsky, R.D., and Colby, J.P. The cost effectiveness of prenatal care in reducing low birth weight in New Hampshire. *Health Services Research* (1989) 24,5:580–98.

The Role of Lifestyle in Preventing Low Birth Weight

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Abstract

Lifestyle behaviors such as cigarette smoking, weight gain during pregnancy, and use of other drugs play an important role in determining fetal growth. The relationship between lifestyle risk factors and low birth weight is complex and is affected by psychosocial, economic, and biological factors. Cigarette smoking is the largest known risk factor for low birth weight. Approximately 20% of all low birth weight could be avoided if women did not smoke during pregnancy. Reducing heavy use of alcohol and other drugs during pregnancy could also reduce the rate of low birth weight births. Pregnancy and the prospect of pregnancy provide an important window of opportunity to improve women's health and the health of children. The adoption before or during pregnancy of more healthful lifestyle behaviors, such as ceasing to smoke, eating an adequate diet and gaining enough weight during pregnancy, and ceasing heavy drug use, can positively affect the long-term health of women and the health of their infants. Detrimental lifestyles can be modified, but successful modification will require large-scale societal changes. In the United States, these societal changes should include a focus on preventive health, family-centered workplace policies, and changes in social norms.

Many of the known risk factors associated with low birth weight, such as socioeconomic status, ethnicity, genetic makeup, and obstetric history, are not within a woman's immediate control. However, there are things that a woman can do to improve her chances of having a normal, healthy child. Lifestyle behaviors, such as cigarette smoking, use of other drugs, and nutrition, play an important role in determining fetal growth. Detrimental habits can be modified, but successful modification requires more than just a dose of individual "self control." Stopping lifelong addictive behaviors is very difficult, and a woman who suffers from them requires support and assistance not only from family members and individuals close to her, but also from the health care system and society.

The relationship between lifestyle risk factors and low birth weight is very complex and is affected by psychosocial, socio-

economic, and biological factors. While it is important to describe the independent effects of different behavioral and socio-

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economic risk factors, we must bear in mind that these factors are not isolated events in women's lives, but are a part of many interrelated complex behaviors and environmental risks. Factors associated with the perinatal health of women and children include demographic factors, medical risks, and maternal behaviors. These risk factors may influence maternal and infant health directly (in terms of physiology) or indirectly (in terms of health behavior). In this article we focus

There are things that a woman can do to improve her chances of having a normal, healthy child.

primarily on lifestyle behavioral risk factors that are amenable to change and that, if modified before or during pregnancy, can improve the likelihood of the delivery of a full-term healthy infant of appropriate size.

Demographic Factors

Socioeconomic status and race/ethnicity are indicators of complex linkages among environmental events, psychological states, and physiologic factors which may lead to low birth weight or preterm delivery. While we do not fully understand the specific biological pathways responsible, we do know that a woman's social and economic status will influence her general health and access to resources. (See the article by Hughes and Simpson in this journal issue for a detailed analysis of the effects of social factors on low birth weight.) In this section, we review the effects of some demographic indicators.

Socioeconomic Status

Low birth weight and infant mortality are closely related to socioeconomic disadvantage. Socioeconomic status, however, is difficult to measure accurately. Educational attainment, marital status, maternal age, and income are interrelated factors and are often used to approximate socioeconomic status, but no single factor truly measures its underlying influence.

Maternal education, maternal age, and marital status are all reflective of socioeconomic status and predictive of low birth weight. Twenty-four percent of the births in 1989 were to women with less than a high school education.¹ Low educational

attainment is associated with higher rates of low birth weight.² For example, relative to college graduates, white women with less than a high school education were 50% more likely to have babies with very low birth weight (less than 1,500 grams, or 3 pounds, 5 ounces) and more than twice as likely to have babies with moderately low birth weight (between 1,500 grams and 2,500 grams, or 3 pounds, 5 ounces and 5 pounds, 8 ounces) than were women who graduated from college.² Teenage mothers are at greater risk of having a low birth weight baby than are mothers aged 25 to 34.¹ However, it is not clear if the risk of teenage childbearing is due to young maternal age or to the low socioeconomic status that often accompanies teenage pregnancy.

The marital status of the mother also appears to be independently associated with the rate of low birth weight,^{2,3} although the relationship appears to vary by maternal age and race. The association of unmarried status with low birth weight is probably strongest for white women over 20 years of age.^{2,4} Marital status may also serve as a marker for the "wantedness" of the child, the economic status of the mother, and the social support that the mother has—all of which are factors that may influence the health of the mother and infant.

It has been hypothesized that economic disadvantage may be a risk factor for low birth weight partly because of the high levels of stress and negative life events that are associated with being poor. Both physical stress and fatigue—particularly related to work during pregnancy—and psychological distress have been implicated.⁵ In addition, stress and negative life events are associated with health behaviors such as smoking.⁶ Social support may act as a moderator or as a buffer from the untoward effects of stressful life experiences and emotional dysfunction.⁷

Race/Ethnicity

The prevalence of low birth weight among white infants is less than half of that for African-American infants (6% and 13%, respectively). This difference reflects a twofold increase of preterm and low birth weight births among African-American mothers.¹ African-American mothers are more likely to have less education, not to be married, and to be younger than white mothers.¹ However, at almost all educational levels and age categories, African-American women have about double the

rates of low birth weight as white women.⁸ This fact indicates that these demographic differences in education, marital status, and age do not account for the large disparity between African Americans and whites in the incidence of low birth weight.

Among infants of Hispanic origin, who represented approximately 15% of live births in 1989, the rate of low birth weight was relatively low (6.1% overall), particularly given that Hispanic women (except Cuban women) had limited educational attainment and were not as likely as non-Hispanic white women to receive prenatal care early in pregnancy.¹

However, Hispanics are a very diverse group, and the low birth weight rates vary considerably by national origin. Low birth weight rates range from 9.4% among Puerto Rican mothers to 5.6% among Cuban mothers. Among Asian infants in 1989, the incidence of low birth weight ranged from 5.1% for Chinese births to 7.3% for Filipino births.¹

It is not known why infants of African-American mothers are twice as likely as all other infants to be born with low birth weights. The etiology of racial disparities in infant mortality and low birth weight is probably multifactorial in nature and is not completely explained by differences in demographics, use of tobacco and other drugs, or medical illnesses.⁹ During the primary childbearing years (ages 15 to 29), the general mortality of African-American women exceeds that of white women for virtually every cause of death.

African-American women have higher rates of hypertension, anemia, and low-level lead exposure than other groups,¹⁰ suggesting that the general health status of African-American women may be suboptimal. Infants of African-American foreign-born mothers have lower risks of neonatal mortality than infants of African-American U.S.-born mothers, a relationship that is not seen between foreign- and U.S.-born white women.¹¹ In addition, racial or ethnic differences in familial structure and social networks may affect morbidity and mortality.¹² More research will be needed to clarify the reasons for these disparities.

Nutrition and Weight Gain

Concerns about nutrition during pregnancy fall into two basic areas, maternal weight gain and nutrient intake, both of which can potentially affect the health of

the mother and infant. As with other lifestyle factors, a woman's nutrition and weight gain are closely linked to her socioeconomic status, cigarette smoking, and other health-related behaviors.

Maternal Weight Gain

Maternal weight gain during pregnancy results from a variety of factors, including maternal dietary intake, prepregnancy weight and height, length of gestation, and size of the fetus. The mother's prepregnancy weight and height are, in turn, a consequence of her genetic makeup, past nutritional status, and environmental factors. The relationship between a woman's caloric intake during pregnancy and her infant's birth weight is complex and is moderated through maternal weight gain and other mechanisms during pregnancy.^{13,14}

Epidemiologic evidence has demonstrated a nearly linear association between maternal weight gain during pregnancy and birth weight,^{15,16} and an inverse relationship to the rate of low birth weight.¹⁶ It comes as no surprise that maternal weight gain during pregnancy is highly correlated with the birth weight of the infant because a large proportion of the weight gain is due to the growth of the fetus itself. Women with total weight gains of 22 pounds (10 kilograms) or less were two to three times more likely to have growth-retarded full-term babies than were women with a gain of more than 22 pounds. Once corrected for the duration

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of pregnancy, the relationship between weight gain and preterm delivery is uncertain.^{17,18}

On average, women gain about 30 pounds during pregnancy. Teenage mothers, older mothers, unmarried mothers, and mothers with less than a high school education are most likely to have low or inadequate weight gain during pregnancy. Even after accounting for gestational age and socioeconomic status, African-American mothers gain less weight than white mothers (28 versus 31 pounds).¹⁹ It has

been estimated that from 15% to 33% of women gain an inadequate amount of weight (less than 22 pounds) during pregnancy.^{13,19} Low weight gain may in part be the result of outdated medical advice and personal beliefs. In one study, one-quarter of the pregnant women believed that they should not gain more than 20 pounds during pregnancy.²⁰ In addition, belief that a smaller baby is easier to deliver and thus that weight gain and fetal birth weight

cal nutrient requirements. Members of the National Academy of Sciences recently reviewed the available literature on dietary intake of nutrients and minerals among pregnant women. They found that the energy intake (calories) for U.S. women was consistently below recommended levels and that the amount of important vitamins and minerals in their diet was also substantially lower than the recommended daily allowance. On average, intakes of protein, riboflavin, vitamin B-12, niacin, and vitamin C exceeded the recommended daily allowance.²⁷

Smoking during pregnancy has been linked to 20% to 30% of low birth weight births.

should be limited influences the amount of weight gained by some women.²¹

While higher maternal weight gain is linked with healthier fetal weight gains, women and clinicians are concerned that women may retain weight after delivery and be at greater risk for obesity. Recent studies have shown that weight retention following delivery increased as weight gain increased, and African-American women retained more weight than white women with comparable weight gains during pregnancy (7.2 versus 1.6 pounds).²² Thus, weight management programs would be appropriate for some women after delivery, but not during pregnancy.

Diet and Nutrient Intake

During pregnancy, the need for calories and nutrients, such as protein, iron, folate, and the other B vitamins, is increased to meet the demands of the fetus as well as the expansion of maternal tissues that support the fetus. As noted by Nathanielsz in this journal issue, the nutritional needs of the fetus are second only to the needs of the mother's brain. Thus, it is important for a pregnant woman to have a well-balanced, nutritious diet to meet the changing needs of her body and her fetus. Unfortunately, the direct relationship between specific vitamins and minerals and low birth weight is unclear, and controversy exists over the association between maternal hematocrit levels (which is a marker for anemia) and preterm birth.²³⁻²⁶

A pregnant woman's current nutritional status is determined by her prepregnant nutritional status, her current intake of nutrients, and her individual physiologi-

cal nutrient requirements. Members of the National Academy of Sciences recently reviewed the available literature on dietary intake of nutrients and minerals among pregnant women. They found that the energy intake (calories) for U.S. women was consistently below recommended levels and that the amount of important vitamins and minerals in their diet was also substantially lower than the recommended daily allowance. On average, intakes of protein, riboflavin, vitamin B-12, niacin, and vitamin C exceeded the recommended daily allowance.²⁷

Women at particular risk of nutritional inadequacy during pregnancy may require nutritional counseling. Groups at risk include women voluntarily restricting caloric intake or dieting; pregnant adolescents; women with low income or limited food budgets; women with eating patterns or practices that require balancing food choices, such as strict vegetarians; women with emotional illness; smokers; women with poor knowledge of nutrition due to lack of education or illiteracy; and women with special difficulties in food resource management because of limited physical abilities and poor cooking or budgeting skills.²⁸

Lifestyle Choices: Cigarette Smoking, Alcohol, Caffeine, and Illicit Drugs

Cigarette Smoking

Since the 1970s, the Surgeon General has reported that cigarette smoking during pregnancy is linked to fetal growth retardation and to infant mortality.²⁹ Smoking during pregnancy has been linked to 20% to 30% of low birth weight births and 10% of fetal and infant deaths.³⁰ Cigarette smoking is unequivocally the largest and most important known modifiable risk factor for low birth weight and infant death.

Approximately 20% to 25% of American women smoke cigarettes during pregnancy.^{31,32} White, young, unmarried, and unemployed women, as well as women with fewer than 12 years of education and low socioeconomic status, are more likely to smoke during pregnancy, compared with nonwhite, older, married women with more than 12 years of education and higher socioeconomic status.^{27,30,33,34} For example, 35% of mothers with less than a high school education smoke compared with 5% of college graduates.³⁵

Smoking retards fetal growth. Birth weight is reduced by 150 to 320 grams (5.3 to 11.4 ounces) in infants born to smokers compared with those born to nonsmokers.³⁶ It has been consistently reported that, even after controlling other factors, women who smoke are about twice as likely to deliver a low birth weight baby as are women who do not smoke.³⁷ A dose-response relationship exists between the amount smoked and birth weight: the percent of low birth weight births increases with increasing number of cigarettes smoked during pregnancy. In addition, exposure to environmental cigarette smoke has also been associated with low birth weight.³⁸ Preterm birth is associated with smoking, but the association is weak compared with the association between low birth weight and smoking.^{9,37} Cigarette smoking during pregnancy may account for up to 14% of preterm deliveries.³⁷

Studies of women who quit cigarette smoking at almost any point during pregnancy show lower rates of low birth weight. Most fetal growth takes place in the last trimester, so that quitting early in pregnancy can decrease the negative effect of smoking on birth weight.³³ Quitting even as late as the seventh or eighth month has a positive impact on birth weight.³⁹

Overall, about one-quarter of women who smoke prior to pregnancy quit upon learning of their pregnancies, and an additional one-third reduce the number of cigarettes they smoke.^{33,40} Older women and more educated women are more likely to quit smoking during pregnancy.⁴¹ Light smokers are more likely to quit smoking than heavier smokers. Heavier smokers are likely to reduce the amount they smoke, but are unlikely to quit.⁴² Social support appears to be a critical factor in changing smoking behavior.⁴⁰

Even among women who do quit smoking during pregnancy, about a third will relapse before childbirth.⁴³ In addition, nearly 80% of women who stop smoking during pregnancy relapse within one year after the delivery.⁴⁰ These high relapse rates reflect the physiological addictive nature of nicotine. While 57% of the pregnant smokers in one study were able to decrease their intake, 40% "tried and failed" to reduce.⁴⁴ Of women who both drank and smoked before pregnancy, fewer women were able to decrease or quit smoking than drinking, despite feelings of social pressure to quit and feelings of guilt at continuing to smoke.⁴⁴ The high recidi-

vism rate after childbirth also reflects diminished maternal contact with the health care system as health care provision shifts from obstetrics to pediatrics.⁴⁵

The bulk of evidence shows a clear and consistent association between low birth weight (primarily due to growth retardation, not preterm birth) and infant mortality and smoking during pregnancy. Smoking also impacts on other aspects of the health status of women and infants. Smoking has been linked to long-term effects in infants such as physical, mental, and cognitive impairments.^{46,47} The linkages between smoking and illnesses, such as cancer and cardiovascular and respiratory disease, are well known.⁴⁸ In addition, research on the effects of passive smoke indicates an increased frequency of respiratory and ear infections among infants and children exposed to this smoke.^{33,49}

Alcohol Use

Alcohol use during pregnancy has long been associated with both short- and long-term negative health effects for infants. Alcohol abuse during pregnancy is clearly related to a series of congenital malforma-

tions described as fetal alcohol syndrome. However, the effects of moderate drinking on the fetus are not well established. Alcohol use among women of childbearing age and, specifically, among pregnant women has apparently declined significantly in the past decades.⁴⁴ This decreasing trend has generally been confined to more educated and older women. However, there has been little or no change in drinking during pregnancy among smokers, younger women, and women with less than a high school education.⁵⁰

Heavy Drinking During Pregnancy

Numerous studies report an association between chronic alcohol abuse and a series of fetal malformations. Fetal alcohol syndrome is characterized by a pattern of severe birth defects related to alcohol use during pregnancy which include prenatal and postnatal growth retardation, central nervous system disorders, and distinct abnormal craniofacial features.⁵¹ Heavy alcohol consumption has been cited as the leading preventable cause of mental retardation worldwide.⁵² It has been estimated that the prevalence of fetal alcohol syndrome is 1 to 3 per 1,000 live births with a significantly increased rate among alco-

grams (about 7 ounces) less than the infants of women who consumed six or fewer drinks per week.⁵⁵

Moderate Drinking During Pregnancy

While the effects of heavy daily drinking are well documented, the impact of moderate drinking is not as well established. Approximately 40% to 60% of pregnant women consume one drink or less a day. Alcohol use exceeding one drink daily ranges from 3% to 13%. Abstinence levels in pregnant women have been reported to range from 16% to 53%.^{50,54,56} Women who consumed less than one alcoholic drink per day had only an 11% increased chance of delivering a growth-retarded infant.⁵⁴ Decrements in birth weight from 32 to 225 grams (1.1 to 8 ounces) have been reported for children born to women who drank one to three drinks daily.^{55,57} Some studies with long-term follow-up have reported deleterious short-term effects and long-term effects, such as growth, mental, and motor delays, for infants of mothers who drink alcohol during pregnancy.^{58,59} However, a number of studies demonstrate insignificant or no effects of "low to moderate" intake on growth at birth⁶⁰ and at four and five years of age.^{58,61} The role of binge drinking is unknown.

Profile of the Pregnant Drinker

The profile of the pregnant drinker varies by the type of drinking. Any alcohol use during pregnancy is associated with older, white, professional, college-educated women with few previous children. Drinkers are also more likely to be unmarried and to smoke than are nondrinkers.⁵⁰ However, heavier alcohol use, in excess of two drinks daily, has been associated with African-American and Hispanic race/ethnicity, less than a high school education, and multiparity. Conversely, women who abstained during pregnancy were more likely to be younger, African-American, and/or of moderate income.⁶²

During pregnancy, many women reduce their drinking⁶³ with decreases occurring in all types of drinkers.⁶⁴ In addition, as pregnancy advances, the proportion of women drinking decreases. In one study, 55% of women drank in the week prior to conception, 50% drank after 32 weeks, and only 20% drank in the last week of their pregnancies.⁶⁵

Many of the studies investigating the relationship of maternal alcohol use to fetal effects suffer from methodologic problems common to substance use re-

Heavy alcohol consumption has been cited as the leading preventable cause of mental retardation worldwide.

holics of 59 per 1,000 live births. Prenatally alcohol-exposed babies with birth defects who do not meet all required criteria for the syndrome are categorized as having fetal alcohol effects. The prevalence of fetal alcohol effects may be threefold that of fetal alcohol syndrome.⁵²

The children of women who continued to drink an average of greater than one drink daily throughout their pregnancies are significantly smaller, shorter, and have smaller head circumferences than infants of control mothers who stop drinking.⁵³ The risk of low birth weight to women drinking three to five drinks per day was increased twofold over nondrinking mothers and almost threefold for those drinking six or more drinks daily when compared with women who did not drink.⁵⁴ A study of French women showed that those who consumed 35 drinks or more a week gave birth to infants that weighed 202

search. Most of the studies rely on self-reporting which, because of the stigma attached to alcohol use during pregnancy, may be inaccurate. Studies of drug use also often fail to consider other important factors, such as maternal nutrition, general health, or marijuana use. In addition, the usual dose, frequency of intake, and timing of drinking during pregnancy may result in different consequences, but this information is often lacking.

Caffeine Consumption

Caffeine is one of the most commonly used drugs. At least 52% of people in the United States drink coffee, 29% drink tea, and 58% consume soft drinks.⁶⁶ Caffeine is most commonly consumed in beverages such as coffee, tea, and soft drinks; eaten in the form of chocolate; and also taken as part of various prescription and nonprescription drugs. No consistent associations between caffeine and low birth weight or preterm birth have been observed.⁶⁷ Most studies have found no association between caffeine use and low birth weight, but some studies report positive yet inconsistent associations.⁶⁷ Several studies have found an interaction between caffeine and cigarette smoking, where the adverse effects of caffeine were observed only among smokers. The existence of such an interaction may help to explain the conflicting results.

Illicit Drug Use

In recent years, the rise in use of illegal drugs, particularly prenatal drug and cocaine, or "crack," use has received extensive coverage in the popular press and sparked many investigations. Prenatal cocaine and heroin abuse are clearly associated with adverse birth outcomes. Other factors in a drug addict's lifestyle, including malnutrition, sexually transmitted diseases, and polysubstance abuse, may contribute to an increased risk of adverse pregnancy outcome and often complicate the ability to examine the effects of individual drugs. The effect of marijuana use on the health of women and their infants is not as clear, nor are the effects of the occasional use of cocaine and other drugs.

Several methodologic problems hinder the interpretation and generalizability of much of the research on both the prevalence and effects of prenatal drug exposure. Studies are often based on small, nonrepresentative samples of mothers, and the bulk of the literature regarding illicit drug use relies on self-reporting. It is difficult to elicit valid information about

illegal drug use, and a significant amount of underreporting probably takes place.⁶⁸ It is also unclear whether some of the effects of drug use are due to fetal drug exposure or to the generally poorer health and limited prenatal care of many addicted women. Finally, most research has been conducted with low-income urban women who are often in poorer health and under greater stress than their middle-class counterparts. The timing of drug use during the course of pregnancy and the dosage undoubtedly influences the consequences of the actions. However, most studies have been unable to characterize

Prenatal cocaine and heroin abuse are clearly associated with adverse birth outcomes.

accurately the use of drugs in pregnancy. In addition, interactive effects of illicit drugs with alcohol, tobacco, or other drugs have not as yet been adequately examined.

Despite the limitations of the research, a number of studies have shown significant effects of individual illicit substances on women and infants. Elevated rates of fetal growth retardation, perinatal death, and pregnancy and delivery complications—such as abruptio placentae, high blood pressure, and preeclampsia—have been observed among drug-abusing women and their infants.^{69–73}

Cocaine Use

Maternal cocaine use has been associated with low birth weight, preterm labor, abruptio placentae, and fetal distress.^{68,74,75} Brain damage and genitourinary malformations of the neonate have been reported, as well as fetal hyperthermia, thyroid abnormalities, stroke, and acute cardiac events.⁷⁶ Neurobehavioral effects found in neonates born to cocaine-abusing mothers have also been reported. These effects include decreased interactive behavior and poor organizational response to environmental stimuli.^{72,74}

Marijuana Use

The effects of prenatal marijuana use on pregnancy and infant outcomes are inconclusive. Children exposed to marijuana *in utero* may be smaller than nonexposed infants.⁶⁸ Other reports suggest that preg-

nant women who smoke marijuana are at higher risk of preterm labor, miscarriage, and stillbirth.⁷⁶ However, other studies find no difference between users of marijuana and nonusers in terms of rate of miscarriage, type of presentation at birth, Apgar status, and frequency of complications or major physical anomalies at birth.⁷⁷

Very little is known about the number of women who use drugs while pregnant, their pattern of drug usage during pregnancy, or the intensity of use. The prevalence of illicit drug use among pregnant women has been estimated using state level and hospital-based studies. Based on anonymous urine toxicology analysis combined with self-reporting, the prevalence of drug use among pregnant women has been estimated at 7.5% to 15%.^{78,79}

Cocaine use among pregnant women has been estimated at 2.3% to 3.4%.^{79,80} Regional and hospital-based data report marijuana use during pregnancy in the range of 3% to 12% and opiate (heroin) use in the range of 2% to 4%.^{78,79} Regional data, such as New York City birth certificate data,⁸¹ documented the dramatic increase in cocaine use relative to other drugs during the 1980s.

Figure 1 presents a profile of substance use among one sample of pregnant women.⁶² Extrapolation of the data suggests that about half of all pregnant women may completely abstain from ciga-

tional drug use during pregnancy than were teenagers. The cessation rates were similar by racial/ethnic background and household income.⁶² In another study, 14% of white women who used marijuana stopped using it upon starting prenatal care, as compared with 6% of African-American women.⁸³

Stress, Physical Activity, Employment, Social Support, Violence, and Sexually Transmitted Diseases

As discussed in the previous section on demographic risk factors, physical and psychosocial stress may be associated with low birth weight. Stress is widely cited in the popular literature as a serious risk to mothers and infants, but current research has not characterized its effects. The scientific literature linking stress and anxiety to obstetric outcome has been equivocal, but there is some basis for the notion that maternal emotional distress may be linked to poor reproductive outcome.⁸⁴

Stress

Stress is believed to influence maternal and infant health via changes in neuroendocrine functioning, immune system responses, and health behaviors. Thus, stress may influence pregnancy outcome directly (in terms of physiology) or indirectly (in terms of health behavior). Physiologically, stress has been associated with anxiety and depression.⁸⁵ It has been suggested that anxiety may increase metabolic expenditure and may lead to a lower gestational weight gain or to an anxiety-mediated change in catecholamine or hormonal balance which could provoke preterm labor.³⁷ Maternal psychological stress or emotional distress may interfere with the utilization of prenatal care or co-occur with particular health behaviors such as smoking and alcohol consumption.

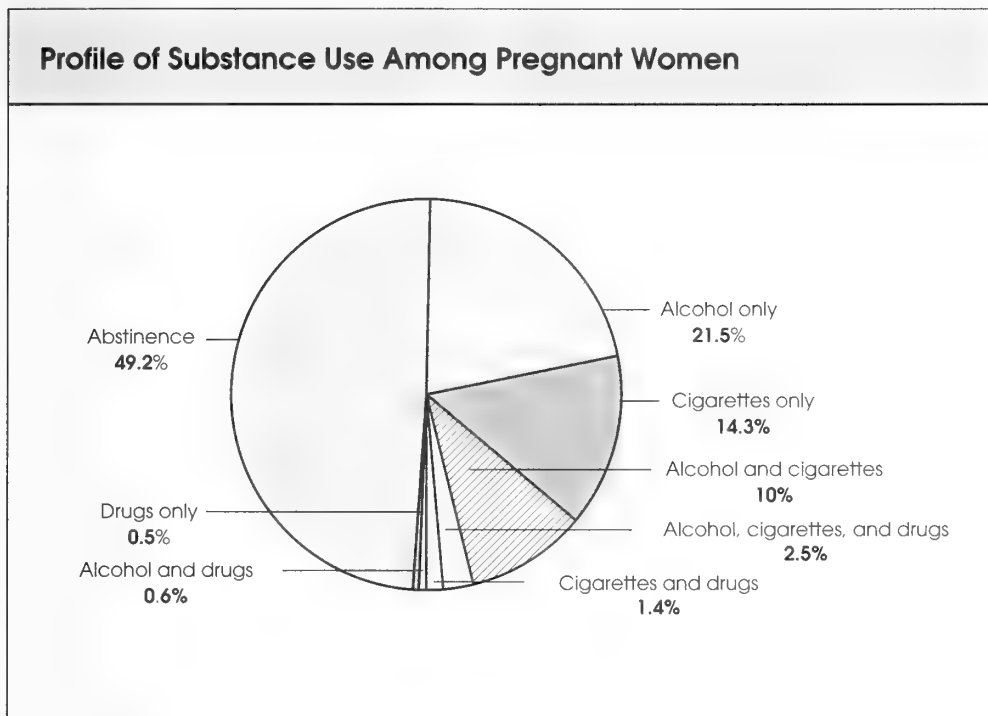
However, the many methodological problems in much of the literature on stress and social support limit the extent to which studies can inform and guide policy and research. The studies are often based on small and ungeneralizable samples, and suffer from possible recall biases, poor reliability, and validity of study instruments and confounding. These difficulties arise from the multifactorial nature of stress and social support and from the

Stress is widely cited in the popular literature as a serious risk to mothers and infants, but current research has not characterized its effects.

rette, alcohol, or drug use. However, approximately 14% of pregnant women engage in two or more high-risk behaviors during pregnancy, with about 2.5% of pregnant women, possibly about 100,000 nationwide, combining smoking, drinking, and recreational drug use.

Recent evidence suggests that, for pregnant women who receive treatment for drug abuse before their third trimester, the risks of low birth weight and preterm birth due to cocaine use may be minimized.⁸² Little is known about which women quit or reduce drug use and why. In one study, college-educated, employed women were more likely to quit recrea-

Figure 1



Source: Adapted from Johnson, S.F., McCarter, R.J., and Ferencz, C. Changes in alcohol, cigarette, and recreational drug use during pregnancy: Implications for intervention. *American Journal of Epidemiology* (1987) 126:4:701. Reprinted with permission of the *American Journal of Epidemiology*.

problems inherent in trying to characterize these poorly understood elements of people's lives.

Physical Activity

Concerns about weight gain and health have resulted in a high level of consciousness about weight control. More than one-third of American women participate in some form of regular physical activity.⁸⁶ Moderate aerobic exercise during pregnancy appears to have little adverse effect on pregnancy outcomes, and the potential benefits of exercise appear to be considerable.⁸⁷ Moderate exercise may be particularly beneficial for women at risk of developing diabetes during pregnancy. Lower levels of blood sugar were observed among diabetic women who were randomly assigned to moderate exercise regimens.⁸⁸ Decreases in the discomforts of pregnancy, improved self-esteem, and reduced tensions were reported among women who had participated in moderate physical conditioning programs during pregnancy.⁸⁹

Employment

The majority of American women are employed during pregnancy.⁹⁰ Women are employed in a wide range of occupations, which have varying degrees of physical and

emotional demands, and varying levels of exposure to employment-related chemicals, radiation, or other toxic substances. Thus, defining a particular "exposure" that characterizes the potential risks of employment has been difficult. In addition, the interrelationship between employment and socioeconomic status is unavoidable. Employed mothers also may accrue positive effects of employment through increased socioeconomic status, better access to medical care, and improved overall lifestyle.⁹¹

In general, the results of studies evaluating the relationship between employment and low birth weight have been inconclusive.⁹² Studies conducted outside the United States have found increased rates of low birth weight and preterm birth among employed women whose jobs required heavy physical labor. However, results of studies conducted in the United States are more mixed and have even demonstrated positive effects of employment. Further advances in this area will be hampered until we are able to better understand the complex relationship among socioeconomic status, employment, stress, and lifestyle.

Domestic Violence

Depending on the population surveyed and the questions asked, the prevalence of battering of pregnant women has been estimated to be 8% to 17%.^{93,94} There is some evidence of low birth weight among women who have been abused during pregnancy,⁹⁵ possibly due to a physical trauma that initiates abruption, infections,

The prevalence of battering of pregnant women has been estimated to be 8% to 17%.

or uterine contractions leading to early onset of labor. In addition, victimization of women may lead to a neglect of chronic medical conditions or to later initiation of prenatal care.⁹⁴

Sexually Transmitted Diseases

Whether or not a woman gets infected with a sexually transmitted disease is highly associated with her sexual behavior and the sexual behavior of her partners. The chance of being infected increases with the number of sexual partners. There is increasing evidence to indicate that various genital infections are associated with low birth weight and preterm delivery.⁹⁶ However, the large number of implicated organisms combined with the numerous genital tract sites that they might infect has made the investigation of sexually transmitted diseases and low birth weight very challenging. Aside from the devastating effects on the fetus of untreated syphilis or gonorrhea, few specific organisms or defined genital tract infections have conclusively been shown to be highly correlated with preterm birth or low birth weight.⁹⁶ Most of the evidence linking genital organisms or infections to birth outcomes has been inconsistent and has shown only a low to moderate association. Clinical trials of antibiotics aimed at removing the organisms or infections have not consistently improved pregnancy outcomes.⁹⁶

Other maternal infections during pregnancy, such as cytomegalovirus, genitourinary infections, pyelonephritis, and HIV, as well as food- or environmentally-borne infections such as toxoplasmosis and listeriosis, may endanger the health of the mother and fetus.^{5,97-99}

Assessing the Impact of Lifestyle Risk Factors on Maternal and Infant Health

In this section, we try to estimate the number of excess low birth weight or small-for-gestational-age babies born due to maternal lifestyle risk factors. As noted earlier, the risk factors for low birth weight described above do not occur as isolated events; rather, they are part of a complex web of social, environmental, and individual factors. To understand the importance of these individual risk factors, we must try to fit them into a framework that represents a realistic picture of what is occurring in women's lives. This task is made more difficult because of our limited knowledge of the many common risk factors and the many potential interactions between factors which would result in a compounding of adverse effects—such as alcohol abuse and heavy cigarette smoking—as well as the role of protective factors.

We started by selecting the risk factors that have a consistent relationship with low birth weight and have been shown to be modifiable. These risk factors are cigarette smoking, alcohol abuse, cocaine abuse, and inadequate weight gain during pregnancy. The data on the prevalence of these factors and the risk incurred were derived from a variety of national and regional studies, and thus the estimates presented reflect the demographic and regional profile of the sample used. The estimates are not the result of a meta-analysis, but are based on published analyses that represent conservative and plausible risk.

We estimated the extra adverse birth outcomes attributed to high-risk lifestyle factors by applying the rate of low birth weight deliveries among cigarette smokers, women with inadequate weight gain, alcohol drinkers, and cocaine users, minus a baseline rate of low birth weight among low-risk women. The effects of reducing stress and exposure to infectious agents cannot be quantified at this time. The numbers we derived are very rough estimates and should be regarded only as order of magnitude estimates.

Prevalence of Lifestyle Risk Factors

From the literature, we extrapolated estimates of the prevalence of high-risk behaviors among pregnant women to the number of live births in the United States

in 1989. Some 20% to 25% of pregnant women, or approximately one million, smoked during pregnancy.^{32,33} (See Figure 2.) Approximately 15%, or about 600,000 nonobese women, may have an inadequate total weight gain of less than 22 pounds during their pregnancy. More than 40% of women may not completely abstain from alcohol but consume less than one drink per day during pregnancy; about 3%, or 120,000 women, may have one or more drinks per day.⁵⁴ Approximately 105,000, or 2.6% of women, may use cocaine around the time of delivery.⁷⁹

Excess Adverse Birth Outcomes

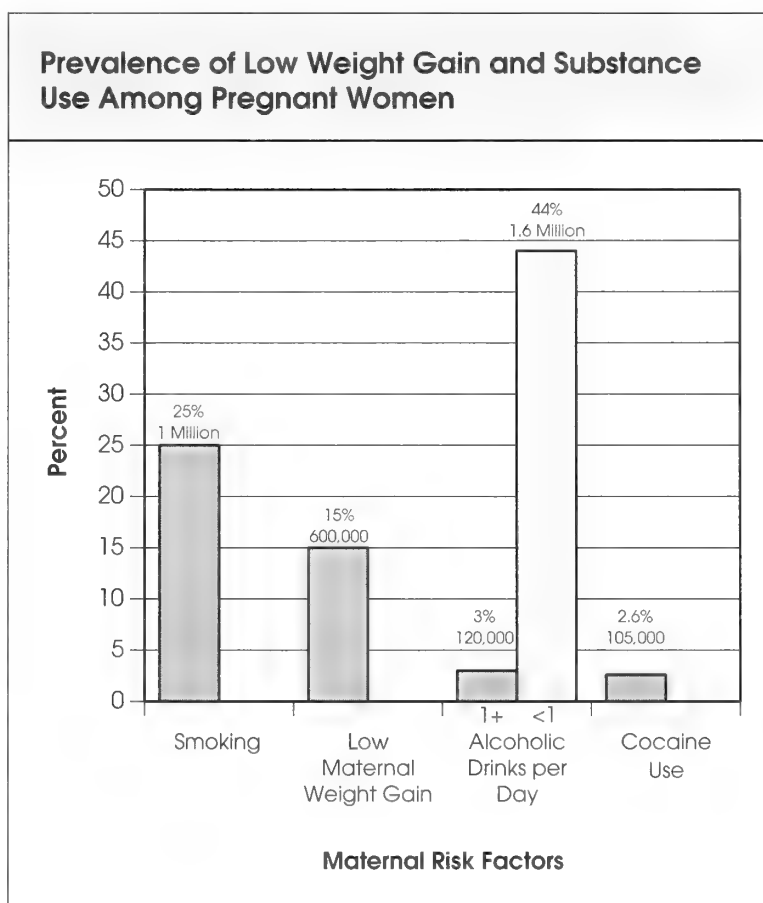
In 1990, there were 4,158,212 births in the United States, and 6.97% (approximately 290,000) of these infants were born low birth weight.¹⁰⁰ It comes as no surprise that reducing cigarette smoking has the largest potential to reduce the incidence of low birth weight. Approximately 48,000 low birth weight births could have been prevented if women had not smoked during pregnancy.

Women who failed to gain adequate weight (less than 22 pounds) by term gave birth to approximately 22,000 extra low birth weight babies who were born at full term. Approximately 14,000 infants a year may be born small for their gestational age due to maternal alcohol consumption, and 10,000 excess low birth weight births could be attributed to prenatal cocaine abuse.

The low birth weight births that are potentially preventable due to smoking, inadequate weight gain, and alcohol use would generally reduce the number of infants who were born too small due to growth retardation but would have little effect on the number of infants born preterm. The lack of a relationship between these risk factors and preterm birth indicates that little improvement in preterm birth rates could be expected with the elimination of these risk factors.

Our estimates of the number of low birth weight births are very rough and may be inaccurate, as these numbers are only as good as our current knowledge of the true relationships between these risk factors and birth outcomes. The number of low birth weight births estimated to be due to each of these factors cannot simply be added together to derive the total number of births that might be prevented by lifestyle changes because these estimates do not take into consideration the interrela-

Figure 2



Source: Chomitz, V.R., Cheung, L., and Lieberman, E. *Healthy mothers—Healthy beginnings*. A white paper prepared by the Center for Health Communication, Harvard School of Public Health. Boston: President and Fellows of Harvard College, 1992.

tionships among the risk factors. For example, a women who is a heavy smoker and drinker would be counted twice in these calculations.

Directions for Future Research: Identifying Barriers to Change

Women face systemic, psychosocial, biological, or knowledge and attitudinal barriers to lifestyle changes. Further research must identify successful strategies for influencing behaviors. Figure 3 illustrates the complexity and interrelationship of common barriers to improving prenatal care and nutritional status, and for modifying smoking, drinking, and drug use.

Although some individuals within an economically depressed or stressful situation may be involved in adverse lifestyle behaviors, most women are not. It is therefore important not only to conduct re-

search with those individuals who have less healthy lifestyles, but also to profile and learn from those who, given similar environmental pressures, do not engage in high-risk behaviors or who have been able to change; that is, we must discover the protective strategies or resilience among individuals who are not engaged in adverse lifestyle behaviors, and apply the lessons learned to intervention programs.

Directions for Prevention/Intervention

Pregnancy and the prospect of pregnancy provide a window of opportunity to improve a woman's health before pregnancy, during pregnancy, and after the birth of her child. Pregnancy provides an opportunity for increased contact with the health care system and is associated with a heightened concern regarding health. Moreover, healthier mothers are more likely to provide more healthful beginnings for their children.

The adoption of healthful lifestyle behaviors before or during pregnancy, such as ceasing to smoke cigarettes, eating

Pregnancy and the prospect of pregnancy provide a window of opportunity to improve a woman's health before pregnancy, during pregnancy, and after the birth of her child.

foods that supply adequate nutrition and produce an appropriate pregnancy weight gain, ceasing or reducing alcohol consumption, and ceasing illicit drug use, can also positively affect the long-term health of women, future pregnancy outcomes, and the health of children.

The health of the family, in general, may also be improved through household dietary changes and the reduction of environmental risks such as secondhand smoke. However, it must be reiterated that behaviors should not be isolated from the environment (society, community, and family) that fosters and supports them, and thus a change in the elements within the environment will facilitate an individual's ability to change his or her behavior. Despite the importance of maternal behavior modification to the health of mothers, infants, and families, it is important to

recognize that there are systemic, biological, psychosocial, and belief and attitudinal barriers to behavioral change which women also must overcome. Expecting women simply to change or modify their behavior without support and attention from the health care system, society, and influential people in their lives is unrealistic and may help to foster the belief that women are solely to blame for undesirable behaviors.

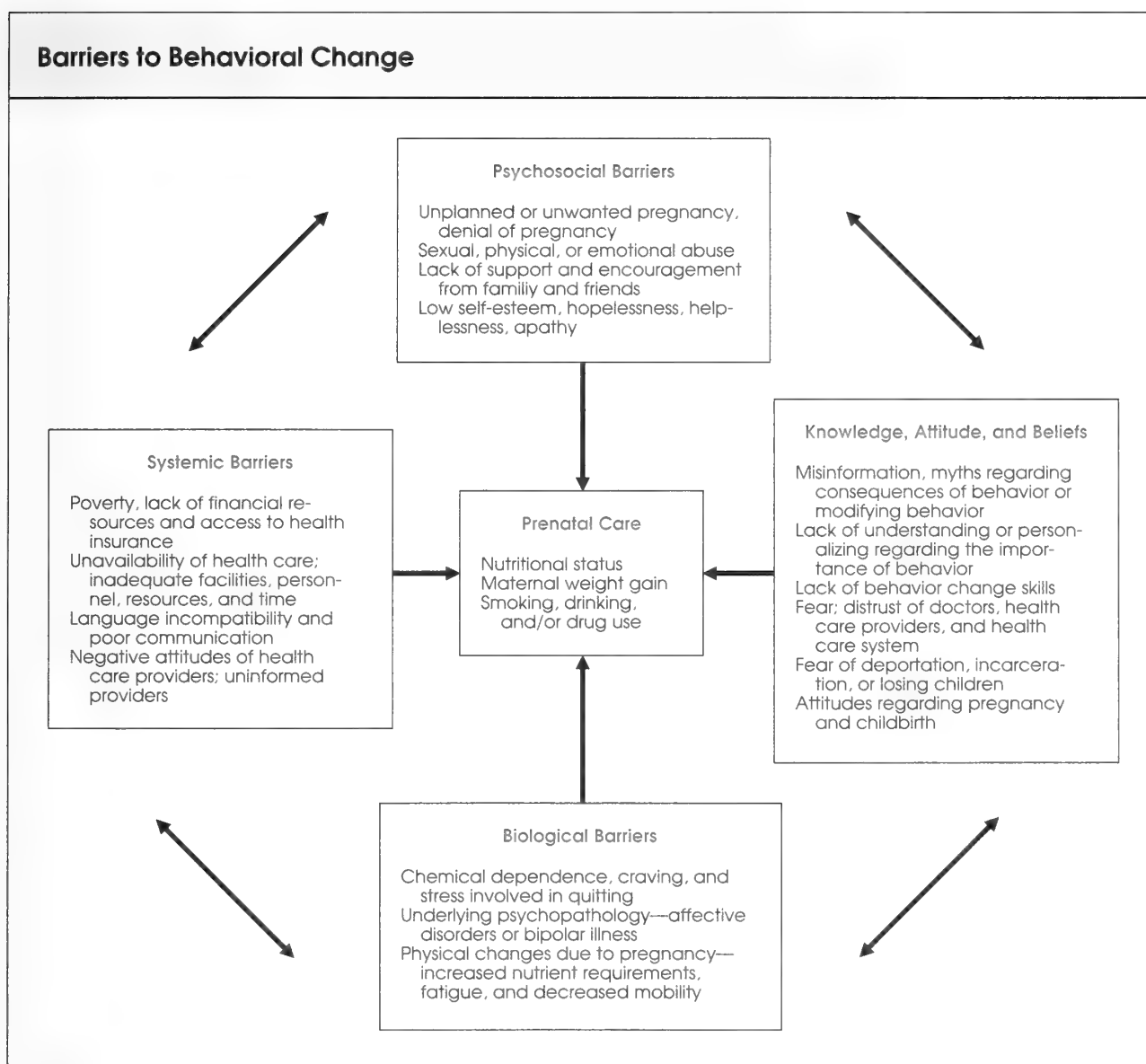
Barriers to successful intervention will not be overcome in the short term and will require both system-level reform and individual efforts. Many women who smoke, engage in high-risk behaviors, eat poorly, or lack access to health care also live surrounded by poverty and violence, and go without adequate housing or employment. Under such circumstances, living a healthful lifestyle may not be a priority compared with day-to-day survival.

Overcoming these social circumstances will require increased access and availability to quality health care, as well as other affiliated resources and facilities such as child care, social services, law enforcement services, affordable and quality food, transportation, and maternity provisions during employment.

Finding ways to improve maternal and infant health and decrease the low birth weight rate is difficult, at least in part because the known causes of low birth weight are multifactorial, and much of the etiology remains unknown. The independent effects of economic disadvantage and inadequate health care coverage on maternal and infant health are difficult to isolate. In addition, medical risk factors that are identified and managed either before or during pregnancy can positively influence the health of women and their infants. Thus, linking women to continuous health care early in pregnancy or, ideally, before conception is a high priority for intervention.

Health promotion efforts aimed at improving infant health must do so by improving women's health. Improving women's health before, during, and after pregnancy is the key to reducing the human and economic costs associated with infant mortality and morbidity. To improve both women's and infants' health, efforts must target long-term, societal elements that involve policy or legislative changes.

Figure 3



Source: Center for Health Communication, Harvard School of Public Health.

These efforts should include an emphasis on preventive health care services, family-oriented work site options, changes in social norms, and individual behavior modification.

Strategies that can reduce the burden of low birth weight do exist. The public and private sectors must work together to define, develop, and implement these strategies.

1. National Center for Health Statistics. *Advance report of final natality statistics, 1991*. Monthly Vital Statistics Report, Vol. 42, No. 3, Suppl. Hyattsville, MD: Public Health Service, September 9, 1993.
2. Kleinman, J., and Kessel, S. Racial differences in low birthweight: Trends and risk factors. *New England Journal of Medicine* (1987) 317,12:749–53.
3. Ahmed, F. Unmarried mothers as a high-risk group for adverse pregnancy outcomes. *Journal of Community Health* (1990) 15,1:35–44.

4. Bennett, T. Marital status and infant health outcomes. *Social Science Medicine* (1992) 35,9:1179–87.
5. Institute of Medicine, Committee to Study the Prevention of Low Birthweight. *Preventing low birthweight*. Washington, DC: National Academy Press, 1985.
6. McCormick, M.C., Brooks-Gunn, J., Shorter, T., et al. Factors associated with smoking in low income pregnant women: Relationship to birthweight, stressful life events, social support, health behaviors, and mental distress. *Journal of Clinical Epidemiology* (1990) 43:441–48.
7. Brooks-Gunn, J. Support and stress during pregnancy: What do they tell us about low birthweight? In *Advances in the prevention of low birthweight: An international symposium*. H. Berendes, S. Kessel, and S. Yaffe, eds. Washington, DC: National Center for Education in Maternal and Child Health, 1991, pp. 39–60.
8. Collins, Jr., J.W., and David, R.J. The differential effect of traditional risk factors on infant birthweight among blacks and whites in Chicago. *American Journal of Public Health* (1990) 80,6:679.
9. Shiono, P., Klebanoff, M., and Rhoads, G. Smoking and drinking during pregnancy. *Journal of the American Medical Association* (1986) 255:82–84.
10. Geronimus, A.T., and Bound, J. Black/white differences in women's reproductive-related health status: Evidence from vital statistics. *Demography* (1990) 27,3:457–66.
11. Kleinman, J., Fingerhut, L.A., and Prager, K. Differences in infant mortality by race, nativity status, and other maternal characteristics. *American Journal of Diseases of Children* (1991) 145:194–99.
12. Moss, N. Demographic and behavioral sciences five year research plan. Draft. Bethesda, MD: National Institute of Child Health and Human Development, 1991.
13. Scholl, T., Hediger, M., Khoo, C., et al. Maternal weight gain, diet and infant birth weight: Correlations during adolescent pregnancy. *Journal of Clinical Epidemiology* (1991) 44:423–28.
14. Susser, M. Maternal weight gain, infant birth weight, and diet: Causal sequences. *American Journal of Clinical Nutrition* (1991) 53,6:1384–96.
15. Kleinman, J. *Maternal weight gain during pregnancy: Determinants and consequences*. Working Paper No. 33. Hyattsville, MD: National Center for Health Statistics, 1990.
16. Luke, B., Dickinson, C., and Petrie, R.H. Intrauterine growth: Correlations of maternal nutritional status and rate of gestational weight gain. *European Journal of Obstetrics, Gynecology, and Reproductive Biology* (1981) 12:113–21.
17. Kramer, M.S., McLean, F.H., Eason, E.L., and Usher, R.H. Maternal nutrition and spontaneous preterm birth. *American Journal of Epidemiology* (1992) 136:574–83.
18. Kramer, M.S., Coates, A.L., Michoud, M., and Hamilton, E.F. Maternal nutrition and idiopathic preterm labor. *Pediatric Research* (1994) 35,4:277A.
19. National Center for Health Statistics. *Advance report of maternal and infant health data from the birth certificate, 1990*. Monthly Vital Statistics Report, Vol. 42, No. 2, Suppl. Hyattsville, MD: Public Health Service, July 8, 1993.
20. Carruth, B.R., and Skinner, J.D. Practitioners beware: Regional differences in beliefs about nutrition during pregnancy. *Journal of the American Dietetic Association* (1991) 91,4:435–40.
21. Chez, R. Weight gain during pregnancy. *American Journal of Public Health* (1986) 76:1390–91.
22. Keppel, K.G., and Taffel, S.M. Pregnancy-related weight gain and retention: Implications of the 1990 Institute of Medicine Guidelines. *American Journal of Public Health* (1993) 83:1100–1103.
23. Klein, L. Premature birth and maternal prenatal anemia. *American Journal of Obstetrics and Gynecology* (1962) 83,5:588–90.
24. Klebanoff, M.A., Shiono, P.H., Selby, J.V., et al. Anemia and spontaneous preterm birth. *American Journal of Obstetrics and Gynecology* (1991) 164:59–63.

25. Lieberman, E., Ryan, K., Monson, R.R., and Schoenbaum, S.C. Association of maternal hematocrit with premature labor. *American Journal of Obstetrics and Gynecology* (1988) 159:107–14.
26. Klebanoff, M., and Shiono, P.H. Facts and artifacts about anemia and preterm birth. *Journal of the American Medical Association* (1989) 262:511–15.
27. Institute of Medicine, Subcommittee on Nutritional Status and Weight Gain During Pregnancy. *Nutrition during pregnancy*. Washington, DC: National Academy Press, 1990.
28. Dwyer, J. Impact of maternal nutrition on infant health. *Medical Times* (1983) 111:30–38.
29. U.S. Department of Health, Education, and Welfare. *The health consequences of smoking*. DHEW/HSM 73-8704. Washington, DC: DHEW, 1973.
30. Kleinman, J., and Madans, J.H. The effects of maternal smoking, physical stature, and educational attainment on the incidence of low birth weight. *American Journal of Epidemiology* (1985) 121:832–55.
31. National Center for Health Statistics. *Advance report of new data from the 1989 birth certificate, 1989: Final data from the National Center for Health Statistics*. Monthly Vital Statistics Report, Vol. 40, No. 12. Hyattsville, MD: Public Health Service, April 15, 1992.
32. National Center for Health Statistics. *Advance report of final mortality statistics, 1989: Final data from the National Center for Health Statistics*. Monthly Vital Statistics Report, Vol. 40, No. 8, Suppl. 2. Hyattsville, MD: Public Health Service, January 7, 1992.
33. U.S. Department of Health and Human Services. *The health benefits of smoking cessation: A report of the Surgeon General*. DHHS/CDC 90-8416. Washington, DC: DHHS, 1990.
34. Cardoza, L.D., Gibb, D.M.F., Studd, J.W.W., and Cooper, D.J. Social and obstetric features associated with smoking in pregnancy. *British Journal of Obstetrics and Gynaecology* (1982) 89:622–27.
35. See note no. 32, National Center for Health Statistics, for mortality statistics in 1989.
36. Butler, N., Goldstein, H., and Ross, E. Cigarette smoking in pregnancy: Its influence on birth weight and perinatal mortality. *British Medical Journal* (1972) 2:127–30.
37. Kramer, M.S. Determinants of low birth weight: Methodological assessment and meta-analysis. *Bulletin of the World Health Organization* (1987) 65:663–737.
38. Martin, T., and Bracken, M. Association of low birth weight with passive smoke exposure in pregnancy. *American Journal of Epidemiology* (1986) 124:633–42.
39. Rush, D., and Cassano, P. Relationship of cigarette smoking and social class to birth weight and perinatal mortality among all births in Britain, 5–11 April 1970. *Journal of Epidemiology and Community Health* (1983) 37:249–55.
40. Wilner, S., Secker-Walker, R.H., Flynn, B.S., et al. How to help the pregnant woman stop smoking. In *Smoking and reproductive health*. M.J. Rosenberg, ed. Littleton, MA: PSG Publishing, 1987, pp. 215–22.
41. Fingerhut, L.A., Kleinman, J.C., and Kendrick, J.S. Smoking before, during, and after pregnancy. *American Journal of Public Health* (1990) 80:541–44.
42. Waterson, E.J., and Murray-Lyon, I.M. Drinking and smoking patterns amongst women attending an antenatal clinic—II. During pregnancy. *Alcohol and Alcoholism* (1989) 24:2:163–73.
43. Windsor, R. *The handbook to plan, implement and evaluate smoking cessation programs for pregnant women*. White Plains, NY: March of Dimes Birth Defects Foundation, 1990.
44. Condon, J.T., and Hilton, C.A. A comparison of smoking and drinking behaviors in pregnant women: Who abstains and why. *Medical Journal of Australia* (1988) 148:381–85.
45. Burns, D., and Pierce, J.P. *Tobacco use in California 1990–1991*. Sacramento: California Department of Health Services, 1992.
46. Brandt, E.N. Smoking and reproductive health. In *Smoking and reproductive health*. M.J. Rosenberg, ed. Littleton, MA: PSG Publishing, 1987, pp. 1–3.

47. Weitzman, M., Gortmaker, S., Walker, D.K., and Sobol, A. Maternal smoking and childhood asthma. *Pediatrics* (1990) 85:505–11.
48. U.S. Department of Health and Human Services. *Reducing the health consequences of smoking: A report of the Surgeon General*. DHHS/CDC 89-8411. Rockville, MD: DHHS, 1989.
49. Samet, J.M., Lewit, E.M., and Warner, K.E. Involuntary smoking and children's health. *The Future of Children* (Winter 1994) 4,3:94–114.
50. Serdula, M., Williamson, D., Kendrick, J., et al. Trends in alcohol consumption by pregnant women. *Journal of the American Medical Association* (1991) 265:876–79.
51. Ouellette, E.M., Rosett, H.L., Rosman, N.P., and Weiner, L. Adverse effects on offspring of maternal alcohol abuse during pregnancy. *New England Journal of Medicine* (1977) 297,10:528–30.
52. Abel, E.L., and Sokol, R.J. Incidence of fetal alcohol syndrome and economic impact of FAS-related anomalies. *Drug and Alcohol Dependence* (1987) 19:51–70.
53. Day, N.L., Jasperse, D., Richardson, G., et al. Prenatal exposure to alcohol: Effect on infant growth and morphologic characteristics. *Pediatrics* (1989) 84,3:536–41.
54. Mills, J.L., Graubard, B.I., Harley, E.E., et al. Maternal alcohol consumption and birth weight: How much drinking during pregnancy is safe? *Journal of the American Medical Association* (1984) 252,14:1875–79.
55. Larroque, B., Kaminski, M., Lelong, N., et al. Effects on birth weight of alcohol and caffeine consumption during pregnancy. *American Journal of Epidemiology* (1993) 137:941–50.
56. Halmesmaki, E., Raivio, K., and Ylikorkala, O. Patterns of alcohol consumption during pregnancy. *Obstetrics and Gynecology* (1987) 69:594–97.
57. Little, R., Asker, R.L., Sampson, P.D., and Renwick, J.H. Fetal growth and moderate drinking in early pregnancy. *American Journal of Epidemiology* (1986) 123,2:270–78.
58. Streissguth, A.P., Bookstein, F.L., Sampson, P.D., and Barr, H.M. Neurobehavioral effects of prenatal alcohol: Part III. PLS analyses of neuropsychologic tests. *Neurotoxicology and Teratology* (1989) 11,5:493–507.
59. Streissguth, A.P., Barr, H.M., and Sampson, P.D. Moderate prenatal alcohol exposure: Effects on child IQ and learning problems at age 7 1/2 years. *Alcoholism, Clinical and Experimental Research* (1990) 14,5:662–69.
60. Walpole, I., Zubrick, S., and Pontre, J. Is there a fetal effect with low to moderate alcohol use before or during pregnancy? *Journal of Epidemiology and Community Health* (1990) 44,4:297–301.
61. Ernhart, C.B., Sokol, R.J., Ager, J.W., et al. Alcohol-related birth defects: Assessing the risk. *Annals of the New York Academy of Sciences* (1989) 562:159–72.
62. Johnson, S.F., McCarter, R.J., and Ferencz, C. Changes in alcohol, cigarette, and recreational drug use during pregnancy: Implications for intervention. *American Journal of Epidemiology* (1987) 126,4:695–702.
63. Little, R., Schultz, F., and Mandell, W. Alcohol consumption during pregnancy. *Journal of Studies on Alcohol* (1976) 37:375–79.
64. Russell, M. Drinking and pregnancy: A review of current research. *New York State Journal of Medicine* (1983) 8:1218–21.
65. See note no. 56, Halmesmaki, Raivio, and Ylikorkala, for more information about alcohol consumption patterns during pregnancy.
66. Lecos, C. Caffeine jitters: Some safety questions remain. *FDA Consumer* (December 1987/January 1988) 21:22.
67. Shiono, P.H., and Klebanoff, M.A. Invited commentary: Caffeine and birth outcomes. *American Journal of Epidemiology* (1993) 137:951–54.
68. Zuckerman, B., Frank, D.A., Hingson, R., et al. Effects of maternal marijuana and cocaine use on fetal growth. *New England Journal of Medicine* (1989) 320:762–68.

69. Zelson, C., Rubio, E., and Wasserman, E. Neonatal narcotic addiction: 10 year observation. *Pediatrics* (1971) 48,2:178–89.
70. Fricker, H., and Segal, S. Narcotic addiction, pregnancy, and the newborn. *American Journal of Diseases of Children* (1978) 132:360–66.
71. Lifschitz, M., Wilson, G., Smith, E., et al. Fetal and postnatal growth of children born to narcotic-dependent women. *Journal of Pediatrics* (1983) 102:686–91.
72. Robins, L.N., and Mills, J.L., Krulewicz, C., and Herman, A.A. Effects of in utero exposure to street drugs. *American Journal of Public Health* (December 1993) 83,12:S9.
73. Oleske, J. Experiences with 118 infants born to narcotic-using mothers. *Clinical Pediatrics* (1977) 16:418–23.
74. Dattel, B.J. Substance abuse in pregnancy. *Seminars in Perinatology* (1990) 14,2:179–87.
75. Bateman, D.A., Ng, S.K.C., Hansen, C.A., and Heagarty, M.C. The effects of intrauterine cocaine exposure in newborns. *American Journal of Public Health* (1993) 83,2:190–93.
76. Office for Substance Abuse Prevention. *Alcohol and other drugs can harm an unborn baby: Fact sheet and resource list*. Rockville, MD: National Clearinghouse for Alcohol and Drug Information, 1989, pp. 1–19.
77. Fried, P.A., and Makin, J.E. Neonatal behavioral correlates of prenatal exposure to marijuana, cigarettes and alcohol in a low risk population. *Neurotoxicology and Teratology* (1986) 9:1–7.
78. Chasnoff, I.J., Landress, H.J., and Barrett, M.E. The prevalence of illicit-drug or alcohol use during pregnancy and discrepancies in mandatory reporting in Pinellas County, Florida. *New England Journal of Medicine* (1990) 322:1202–6.
79. Centers for Disease Control and Prevention. Statewide prevalence of illicit drug use by pregnant women—Rhode Island. *Morbidity and Mortality Weekly Report* (1990) 39,14:225–27.
80. Handler, A., Kistin, N., Davis, F., and Ferré, C. Cocaine use during pregnancy: Perinatal outcomes. *American Journal of Epidemiology* (1991) 133:818–25.
81. Zeitel, L., Bauer, T.A., and Brooks, P. *Infants at risk: Solutions within our reach*. New York: Greater New York March of Dimes/United Hospital Fund of New York, 1991.
82. U.S. General Accounting Office. *Drug abuse: The crack cocaine epidemic: Health consequences and treatment*. HRD-91-55FS. Washington, DC: GAO, 1991.
83. McCaul, M.E., Svikis, D.S., and Feng, T. Pregnancy and addiction: Outcomes and interventions. *Maryland Medical Journal* (1991) 40:995–1001.
84. Newberger, E.H., Barkan, S.E., Lieberman, E.S., et al. Abuse of pregnant women and adverse birth outcome: Current knowledge and implications for practice. *Journal of the American Medical Association* (1992) 267,17:2370–72.
85. McAnarney, E.R., and Stevens-Simon, C. Maternal psychological stress/depression and low birth weight. *American Journal of Diseases of Children* (1990) 144:789–92.
86. Katch, F.I., and McArdle, W.E. *Introduction to nutrition, exercise and health*. 4th ed. Philadelphia: Lea and Febiger, 1993.
87. Dewey, K.G., and McCrory, M.A. Effects of dieting and physical activity on pregnancy and lactation. *American Journal of Clinical Nutrition* (1994) 59:446S–53S.
88. Jovanovic-Peterson, L., Durak, E.P., and Peterson, C.M. Randomized trial of diet versus diet plus cardiovascular conditioning on glucose levels in gestational diabetes. *American Journal of Obstetrics and Gynecology* (1989) 161:415–19.
89. Hall, D.C., and Kaufmann, D.A. Effects of aerobic and strength conditioning on pregnancy outcomes. *American Journal of Obstetrics and Gynecology* (1987) 157:1199–1203.
90. U.S. Bureau of the Census. *Work and family patterns of American women*. Current Population Reports, Series P-23, No. 165. Washington, DC: U.S. Government Printing Office, 1990.
91. Poerksen, A., and Petitti, D.B. Employment and low birth weight in black women. *Social Science and Medicine* (1991) 33:1281–96.

92. Simpson, J.L. Are physical activity and employment related to preterm birth and low birth weight? *American Journal of Obstetrics and Gynecology* (1993) 168:1231–38.
93. Helton, A.S., McFarlane, J., and Anderson, E.T. Battered and pregnant: A prevalence study. *American Journal of Public Health* (1987) 77,10:1337–39.
94. McFarlane, J., Parker, B., Soeken, K., and Bullock, L. Assessing for abuse during pregnancy: Severity and frequency of injuries and associated entry into prenatal care. *Journal of the American Medical Association* (1992) 267,23:3176–78.
95. Bullock, L.F., and McFarlane, J. The birth-weight/battering connection. *American Journal of Nursing* (September 1989):1153–55.
96. Gibbs, R.S., Romero, R., Hillier, S.L., et al. A review of premature birth and subclinical infection. *American Journal of Obstetrics and Gynecology* (1992) 166:1515–28.
97. Carroll, J.C. Chlamydia trachomatis during pregnancy: To screen or not to screen? *Canadian Family Physician* (1993) 39:97–102.
98. Kramer, M.S. The etiology and prevention of low birthweight: Current knowledge and priorities for future research. In *Advances in the prevention of low birthweight: An international symposium*. H. Berendes, S. Kessel, and S. Yaffe, eds. Washington, DC: National Center for Education in Maternal and Child Health, 1991, pp. 25–39.
99. Zygmunt, D.J. Toxoplasma gondii. *Infection Control and Hospital Epidemiology* (1990) 11,4:207–11.
100. Wegman, M.E. Annual summary of vital statistics—1992. *Pediatrics* (1993) 92,6:743–54.

Evaluation of Neonatal Intensive Care Technologies

Jeffrey D. Horbar
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Abstract

The development and dissemination of neonatal intensive care technology has been associated with improved survival for critically ill newborn infants, particularly those with birth weights of less than 1,500 grams (3 pounds, 5 ounces). Despite these advances, there are concerns about the long-term health status of surviving infants and the costs of their initial and subsequent care. In this article, the authors review current evidence for the effectiveness of neonatal intensive care and discuss several approaches to evaluating neonatal intensive care technology. They discuss a four-step process originally proposed by Roper for assessing and improving neonatal intensive care practices which includes (1) monitoring of practices, outcomes, and costs; (2) analysis of variation in practices, outcomes, and costs; (3) assessment of the efficacy of individual interventions, and (4) feedback and education to alter clinical behavior. The authors conclude that organized networks of neonatal intensive care units can play a crucial role in this process.

The development and dissemination of neonatal intensive care technology has been associated with increasing survival for low birth weight infants, particularly those weighing less than 1,500 grams (3 pounds, 5 ounces) at birth. Other factors have also contributed to this trend, including the regionalization of perinatal care, the emergence of subspecialists in maternal-fetal medicine, neonatal medicine, and pediatric surgery, and diagnostic and therapeutic advances in high-risk obstetrics. Despite improvements in survival, however, there are continuing concerns about the high costs of neonatal intensive care and the quality of life of survivors. In this article we will discuss the evaluation of neonatal intensive care technologies and emphasize the role that organized networks of neonatal intensive care units can play in evaluating and continuously improving the effectiveness and efficiency of neonatal intensive care.

Background

Neonatal intensive care for critically ill newborns was introduced in the late 1960s when methods for providing assisted ventilation to small infants were first devel-

oped. Because neonatal intensive care units required specialized personnel and facilities beyond those available at most hospitals, national efforts were made to regionalize their location.¹ This strategy was successful in increasing the availability

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of neonatal intensive care and resulted in improved survival rates for low birth weight infants.² By 1976 there were more than 125 neonatal intensive care units in North America, primarily at major university medical centers.³ There are now reported to be more than 700 such units, including both level 2 and level 3 nurseries.⁴ Clearly, there has been a dramatic increase in the number of neonatal intensive care units. As a result, the majority of newborns receiving intensive care are now treated in smaller nonuniversity hospitals. This trend, called "deregionalization," is discussed in detail in the article by McCormick and Richardson in this journal issue.

Neonatal-perinatal medicine became a board-certified subspecialty of pediatrics in 1975. The training period consists of three years of general pediatric residency

has been accompanied by rapid expansion in the range and complexity of medical, surgical, and diagnostic services provided to critically ill newborns. In 1981, Sinclair and colleagues enumerated some of the specific preventive and therapeutic maneuvers included in neonatal intensive care programs.⁷ They concluded that, although the efficacy of some specific intensive care maneuvers had been validated in randomized controlled trials, the overall effectiveness of neonatal intensive care programs required further evaluation with rigorous scientific methods. Since that article was written, a large number of new intensive care techniques have been introduced. Also, neonatal intensive care has been provided to progressively smaller and less mature infants so that infants at 23 weeks gestational age and 400 grams (14 ounces) birth weight are now receiving intensive care at many institutions.

A representative list of the technologies and procedures that are included in current neonatal intensive care programs is shown in Box 1. This list is not exhaustive but does give an indication of the range of diagnostic and therapeutic measures which are used in modern neonatal intensive care. Most of the specific measures have still not been subjected to rigorous scientific testing, and there is considerable variation among neonatologists in how these techniques are used.

There have been marked declines in neonatal and infant mortality rates coincident with the introduction and refinement of neonatal intensive care.

plus three years of neonatology fellowship in one of 106 approved training programs. All neonatologists who entered training programs after 1989 are required to take a recertification examination in general pediatrics and neonatology every seven years. A survey of perinatal centers performed in 1983 estimated that there were 1,509 physicians practicing neonatology in the United States.⁵ In 1993, the Accreditation Council for Graduate Medical Education listed 528 physicians in neonatal training programs and 2,498 board-certified neonatologists. There is no official estimate of the total number of pediatricians currently practicing neonatology, some of whom are not board certified, but a data base maintained by Abbott Laboratories lists 3,740 individuals interested in neonatology. A survey is being carried out by the American Academy of Pediatrics to gather more accurate data on the number of neonatologists who are actually in practice. These data are important because questions have been raised as to whether there are currently too many neonatologists in the United States as compared with the number in other countries.⁶

The growth in the numbers of neonatologists and neonatal intensive care units

The Impact of Neonatal Intensive Care

Mortality

Several lines of evidence support the hypothesis that neonatal intensive care has resulted in decreased mortality. First, there have been marked declines in neonatal and infant mortality rates coincident with the introduction and refinement of neonatal intensive care.⁸⁻¹⁰ This decline has been almost entirely due to improvements in the survival of very low birth weight infants rather than a decrease in the number of very low birth weight infants.¹⁰ Between 1965 and 1975, neonatal mortality rates decreased by 35%. Because other factors known to affect survival at a given birth weight did not change during this period, Lee and colleagues concluded that improvements in perinatal medical care were responsible.⁸ A more recent drop in infant mortality has been associated with a specific neonatal intensive care practice.¹¹⁻¹³ Between 1989 and 1990, the

Box 1

Neonatal Intensive Care Technologies and Procedures**1. Environmental Control**

incubators
 radiant warmers
 servo-controlled thermoregulation
 heat shields
 plastic wrap
 humidification
 control of noise and light

2. Vascular Access

umbilical artery/vein catheters
 peripheral artery/vein catheters
 central venous catheters
 infusion and syringe pumps

3. Physiologic Monitoring

temperature
 cardiorespiratory
 electrocardiogram
 thoracic impedance
 apnea/bradycardia alarms
 trend monitors
 systemic blood pressure
 oscillometric method
 indwelling artery catheter
 central venous pressure
 oxygenation/ventilation
 arterial blood sampling
 capillary blood sampling
 pulse oximetry
 transcutaneous PO₂, CO₂
 end tidal CO₂
 pulmonary function testing

4. Laboratory Testing

micro sampling methods
 bedside glucose testing
 routine chemistry, hematology, serology
 microbiology
 pulmonary maturity
 genetic analysis
 metabolic screening

5. Diagnostic Imaging

radiography
 ultrasonography
 doppler echocardiography
 CT-scanning
 MRI scanning
 nuclear medicine scanning

6. Nutritional Support

parenteral nutrition

enteral feeding techniques
 special formula
 breast milk supplements
 vitamins
 minerals
 trace elements

7. Blood Products

red blood cells
 white blood cells
 platelets
 plasma
 cryoprecipitate
 coagulation factors
 irradiation of blood products

8. Respiratory Support

supplemental oxygen
 continuous positive airway pressure
 chest physiotherapy
 conventional ventilation
 high-frequency ventilation
 surfactant
 extracorporeal membrane oxygenation

9. Delivery Room Resuscitation**10. Neonatal Pharmacotherapeutics**

diuretics
 xanthines
 steroids
 indomethacin
 antimicrobials
 heparin
 vasopressors
 sedatives/analgesics

11. Phototherapy**12. Neonatal Surgery/Anaesthesia****13. Psychosocial Interventions**

unlimited parental visiting
 parental involvement in care
 skin-to-skin contact
 infant stimulation
 reducing noxious stimuli
 nonnutritive sucking

14. Neonatal Transport

skilled transport teams
 air/ground transport

15. Other Diagnostic Testing

electroencephalogram
 evoked response audiometry

infant mortality rate dropped by 6% (from 9.7 to 9.1/1,000 births). Kleinman estimated that as much as one-half of this change may have been due to the introduction of surfactant therapy, which reduces serious lung disease, into neonatal intensive care.¹¹

The second line of evidence regarding the effect of neonatal intensive care on infant mortality is the observation showing that low birth weight infants born in hospitals with tertiary level neonatal intensive care units have lower mortality rates than infants born in hospitals without such units.¹⁴

Paneth and colleagues found that preterm low birth weight infants born in New York City were at a 24% lower risk of death if they were born at a hospital providing tertiary level neonatal intensive care.¹⁵ Similar findings have been reported for total population cohorts of infants from New York City,¹⁶ several states in the United States,^{17,18} and the Netherlands.¹⁹

Finally, increased access to neonatal intensive care—either because a new neonatal intensive care unit is opened²⁰ or because regionalized neonatal services are instituted²—has been associated with decreases in neonatal mortality. In Hamilton-Wentworth County, Ontario, mortality for very low birth weight infants dropped by nearly 17% after a regional

neonatal intensive care unit was opened in 1973.²⁰

All of these findings suggest that neonatal intensive care has played a role in improving survival for low birth weight infants. Other factors, including regionalized transport systems for high-risk women and infants, advances in obstetrical care and neonatal surgery, and improved training in maternal-fetal and neonatal medicine, have also had an effect.

Long-Term Outcomes

The impact of neonatal intensive care on long-term outcomes for low birth weight infants is more complex. (See the article by Hack, Klein, and Taylor in this journal issue for a detailed discussion of long-term developmental outcomes.) In a case study published in 1987, the Office of Technology Assessment concluded that “neonatal intensive care has contributed to improved longterm developmental outcomes for premature infants. The great decline in mortality among all subgroups of very low birth weight infants over the past 10 years, however, means there are now larger absolute numbers of both seriously handicapped and normal survivors.”²¹ A recent review of population-based registries of cerebral palsy found that one unavoidable side effect of the increasing success of neonatal intensive care is a moderate rise in the childhood prevalence of cerebral palsy.²² In addition

to neurobehavioral disabilities and poor school performance, children born at very low birth weight who survive are also at higher risk for a broad range of other adverse health outcomes at school age.^{23–27} As a result, survivors of neonatal intensive care have significantly increased medical care costs throughout childhood, which may pose a substantial financial burden to their families.^{28,29} These long-term consequences must be carefully balanced against the gains in survival in any evaluation of neonatal intensive care.

Extreme Immaturity

There is considerable uncertainty about the effectiveness of neonatal intensive care for extremely immature infants. Difficult questions arise as attempts are made to identify lower limits of birth weight and gestational age below which neonatal intensive care is either futile or does more harm than good for the individual infant, its family, and society. (For a discussion of these ethical issues, see the article by Tyson in this journal issue.) Based on infants born between 1982 and 1988, Hack and Fanaroff concluded that, with few exceptions, survival is limited to infants with birth weights of 600 grams (1 pound, 5 ounces) or more or to those whose gestational age is at least 24 weeks.³⁰ They found no improvement in the outcomes for such infants between 1982 and 1988. Allen and colleagues, in a study of infants of 22 to 25 weeks gestation born from 1988 to 1991, found that no infants born at 22 weeks gestation survived as compared with 15% of infants born at 23 weeks, 56% born at 24 weeks, and 79% born at 25 weeks gestation.³¹ Only 2% of infants born at 23 weeks gestation survived without severe brain injury as compared with 21% of those born at 24 weeks and 69% of those born at 25 weeks of gestation. Allen and colleagues concluded that aggressive resuscitation and intensive care treatment are indicated for infants born at 25 weeks gestation, but not for those born at 22 weeks gestation. They recommend that, for infants born at 23 or 24 weeks gestation, discussions involving parents, health care providers, and society at large are required. In contrast, in 1991 the law in Japan was amended to lower the limit of viability from 24 to 22 weeks because of increasing numbers of survivors with gestational ages below 24 weeks.^{32,33} Questions about which infants should receive intensive care will become even more pressing as scarce health care

resources are carefully scrutinized and reallocated.

Clinical Evaluation Science

Clinical evaluation science provides a natural framework for evaluating neonatal intensive care. This emerging field, otherwise known as outcome research or medical effectiveness research, uses a variety of analytic techniques to understand the relationships between the structure, process, outcomes, and costs of medical care.³⁴ Clinical evaluation science attempts to identify and explain the variations in the practice and outcomes which have been observed to occur among regions, among hospitals, and among physicians. Ultimately, the goal is to change inappropriate practice patterns by disseminating information to physicians and patients. The Patient Outcome Research Teams sponsored by the Agency for Health Care Policy and Research are a major example of this strategy in action.³⁵

Roper and colleagues have described a four-step process for assessing the effectiveness of medical care and improving clinical practice which illustrates many of the techniques of clinical evaluation science.³⁶ This process includes (1) monitoring of practice, outcomes, and costs, (2) analysis of variations in practice, outcomes, and costs (3) assessment of the

The goal of clinical evaluation science is to change inappropriate practice patterns by disseminating information to physicians and patients.

efficacy of individual interventions, and (4) feedback and education to alter behavior. We will discuss each of these steps as they apply to neonatal intensive care and describe the role that neonatal research networks can play in this process.

Monitoring

Monitoring the medical interventions, outcomes, and costs for large populations requires accurate and timely data collected using uniform definitions. A major barrier to monitoring neonatal intensive care on a large scale is the lack of adequate data sources. In the Medicare population,

for which considerable effectiveness research has been done, monitoring is facilitated by the availability of a universal data base of Medicare claims.

No similar national data sources are available for monitoring outcomes, interventions, and costs for perinatal patients. Studies in perinatal patients have, therefore, relied on vital statistics, linked birth and death certificates, state Medicaid files, medical record reviews, and hospital discharge abstracts.

Unfortunately, these sources often lack the clinical detail necessary to properly monitor neonatal intensive care. A pioneering example of how existing data sources can be used for monitoring neonatal care is the system developed by Williams, which uses linked birth and death certificates, for the state of California.³⁷

The March of Dimes Birth Defects Foundation, in its recent publication, *Toward Improving the Outcome of Pregnancy: The*

Network data bases are now a major resource for monitoring the process and outcomes of neonatal intensive care.

90s and Beyond, recognizes that improved data sources will be crucial to the evaluation of neonatal intensive care.³⁸ Comprehensive perinatal data systems at the state and regional level, which include vital statistics and information about clinical practice, will be needed. As integrated delivery systems are developed under health reform, there will be opportunities to create modern information systems which can be used to assess the effectiveness and costs of neonatal intensive care.

Neonatal Network Data Bases

Currently, data bases maintained by neonatal research networks provide an important source of data for monitoring the practice and outcomes of neonatal intensive care. There are now at least eight such networks collecting information on infants receiving neonatal intensive care (see Box 2).

Two examples of networks with ongoing data bases are the Vermont-Oxford Trials Network³⁹ and the National Institute of Child Health and Human Development (NICHD) Neonatal Research Network.⁴⁰ These networks perform randomized tri-

als^{41–43} and maintain data bases for observational studies. The Vermont-Oxford Trials Network consists of a broad range of university and nonuniversity neonatal units.

Membership is voluntary, most units are small, and participating investigators do not receive salary support for participation. The NICHD Neonatal Research Network consists of large university research centers with network-funded research personnel.

Both of these networks maintain data bases for infants with birth weights below 1,500 grams (3 pounds, 5 ounces). In 1992, the Vermont-Oxford Trials Network collected information about more than 5,000 very low birth weight infants at 68 neonatal units. In 1993, it collected data on more than 6,600 infants at 84 neonatal units.

The NICHD Neonatal Research Network collected data on nearly 3,000 infants at 12 neonatal units in 1992. Combined, these networks represent approximately 20% of all very low birth weight infants born in the United States. Network data bases such as these are now a major resource for monitoring the process and outcomes of neonatal intensive care.

Analysis of Variations

Since 1973, when Wennberg and Gittlesohn demonstrated that there were marked variations in the utilization of surgical procedures among hospital service areas within the state of Vermont, a large body of research has confirmed that both patterns of care and patient outcomes vary among geographic areas and hospitals in ways that cannot be explained by differences in the patient populations which are served.⁴⁴ In addition to large differences in utilization rates for surgical procedures, diagnostic services, and hospital admissions, there is also wide variation in hospital mortality for a number of different medical conditions.⁴⁵

In the following sections, we will review the data concerning variations in interventions and outcomes for neonatal intensive care and discuss approaches to risk adjustment for neonatal patients which may be useful in determining the causes of the observed variations.

Variations in the Use of Interventions

Large variations in the use of prenatal corticosteroids exist despite their proven effectiveness in reducing morbidity and mortality among preterm infants. Corti-

Box 2

Neonatal Research Networks

Name	Contact Person/Address
1. BAPM Perinatal Clinical Trials Group—British Association of Perinatal Medicine	Secretary BAPM c/o Perinatal Trials Service NEPU, Radcliffe Infirmary Oxford, OX2 6HE UK
2. Canadian Perinatal Clinical Trials Network*	W. Fraser, M.D. L'Hopital St. Francois d'Assise 10 Rue de L'Espinay Quebec, G1L 3L5 CANADA
3. International Neonatal Network*	W.O. Tarnow-Mordi, M.D. Department of Child Health Ninewells Hospital and Medical School Dundee, DD1 9SY UK
4. National Perinatal Information Center*	David E. Gagnon, M.P.H. Executive Director One State Street, Suite 102 Providence, RI 02908
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6. Perinatal Trials Service—National Perinatal Epidemiology Unit*	Diana Elbourne, Ph.D. NEPU, Radcliffe Infirmary Oxford, OX2 6HE UK
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costeroid treatment of women at risk for preterm delivery induces lung maturation in the fetus and improves neonatal outcomes.⁴⁶ (For further discussion of the effectiveness of corticosteroids, see the article by Ricciotti in this journal issue.)

There is clear and convincing evidence from numerous randomized controlled trials that antenatal corticosteroid treatment not only reduces the risk of respiratory distress syndrome in preterm infants of treated women but also reduces the risk

Table 1

Percentage of Infants with Selected Interventions: Vermont-Oxford Trials Network, 1992 (5,032 infants weighing 501 to 1,500 grams treated at 68 centers)		
Interventions	Percentage of Infants	
	In Total Network	In Individual Centers ^a
Oxygen	86	81 – 94
Nasal CPAP ^b	33	7 – 53
Ventilator	77	70 – 85
High frequency ventilator	8	0 – 13
Surfactant	54	42 – 63
Steroids for CLD ^c	19	10 – 26
Indomethacin for PDA ^d	76	71 – 90
Surgery for PDA ^d	13	0 – 18

^a Interquartile ranges.
^b CPAP = continuous positive airway pressure.
^c CLD = chronic lung disease.
^d PDA = patent ductus arteriosus. Rates are for those infants with symptomatic PDA.

Source: *The Vermont-Oxford Trials Network 1992 Annual Report*. Burlington, VT: Neonatal Research and Technology Assessment, 1993.

of death and intraventricular hemorrhage.⁴⁷ Despite this evidence, many obstetricians prescribe antenatal steroids infrequently for women at risk for preterm delivery, and some obstetricians do not prescribe them at all. At 73 centers participating in the Vermont-Oxford Trials Network in either 1991 or 1992, 26% of the 8,749 infants weighing 501 to 1,500 grams

infants.⁴⁰ Overall, 16% of infants in the NICHD Network were delivered to women who had received steroids with a range of 1% to 33%.

Reports from these two neonatal networks also document substantial variation among neonatal intensive care units (NICUs) in the use of a number of other postnatal interventions and procedures. Table 1 shows the overall frequencies for selected interventions and their interquartile ranges at 68 centers which participated in the Vermont-Oxford Trials Network in 1992.⁴⁹

The variation persisted even within 250-gram birth weight categories. Data for variation in postnatal interventions are also provided by the NICHD Neonatal Research Network. Methods of delivery room management, use of phototherapy, exchange transfusions, indwelling vascular catheters, and parenteral nutrition all exhibited considerable variation among the NICHD Network Centers.⁴⁰ The persistence of variation within relatively narrow birth weight categories suggests that the variation is due in large part to differences in practice styles among the units.

Reports from these two neonatal networks also document substantial variation among neonatal intensive care units in the use of a number of other postnatal interventions and procedures.

(from 1 pound, 2 ounces to 3 pounds, 5 ounces), were born to women who had received antenatal steroids.⁴⁸ Twenty-five percent of the centers in the network had treatment frequencies of 11% or less; 25% of centers had frequencies of 36% or more; only 10% of centers had frequencies of 60% or more. Data from the NICHD Neonatal Research Network also indicate wide variation in the use of antenatal steroid therapy for very low birth weight in-

Table 2

Percentage of Infants with Selected Outcomes: Vermont-Oxford Trials Network, 1992 (5,032 infants 501 to 1,500 grams at 68 centers)		
Outcomes	Percentage of Infants	
	In Total Network	In Individual Centers ^a
Respiratory distress syndrome	68	59 – 82
Pneumothorax	8	5 – 10
Supplemental oxygen, day 28	37	27 – 44
Patent ductus arteriosus	35	24 – 48
Bacterial sepsis	17	9 – 25
Intraventricular hemorrhage	29	19 – 35
Retinopathy of prematurity	48	34 – 62

^a Interquartile ranges.

Source: *The Vermont-Oxford Trials Network 1992 Annual Report*. Burlington, VT: Neonatal Research and Technology Assessment, 1993.

Variations in Outcomes After Neonatal Intensive Care

As previously discussed, neonatal intensive care has resulted in increased birth-weight-specific survival rates and a decrease in the overall infant mortality rate. Infants born at hospitals with level 3 neonatal intensive care units have lower neonatal mortality than infants born at hospitals without such units.^{15–19} Even among level 3 neonatal intensive care units, however, there are substantial variations in both mortality and morbidity among the survivors.

Avery and colleagues found that the incidence of chronic lung disease in infants weighing 700 to 1,500 grams (from 1 pound, 9 ounces to 3 pounds, 5 ounces) varied significantly among the eight institutions studied even after adjusting for birth weight, race, and gender.⁵⁰ The investigators suggested that the observed variation was due to differences in respiratory care practices among the centers. Horbar, in a study of 11 neonatal intensive care units, found differences among centers both in the frequency of chronic lung disease and in neonatal mortality.⁵¹ Again, the differences persisted after adjustment for birth weight, race, and gender. Kraybill and colleagues, in a survey of 10 neonatal units in North Carolina, found significant differences among centers in the frequency of chronic lung disease.⁵² They also suggested that differences in respira-

tory care practices might explain the findings. Hack and colleagues, reporting for the NICHD Neonatal Research Network, indicate that there are large intercenter differences in morbidity, particularly with respect to chronic lung disease, necrotizing enterocolitis, intraventricular hemorrhage, and jaundice.⁴⁰ Wide variation in most morbidities have also been documented for centers in the Vermont-Oxford Trials Network (see Table 2).⁴⁹

These data suggest that there are differences among neonatal intensive care units with respect to short-term morbidity and mortality. While some of these differences may be due to differences in the way specific outcomes are diagnosed at the different centers, the extent to which they are due to differences in the quality of medical care is unknown. Data regarding variation in long-term neurodevelopmental outcomes and other morbidities among centers are not available.

Risk Adjustment

Variations in the outcomes of hospitalized patients have been used as indicators of the effectiveness of medical care. However, before inferences can be drawn from observed differences in mortality or other outcomes among hospitals, it is necessary to account for differences in case mix. Variation in hospital mortality has three major sources: the underlying risk of a hospital's patient population, the effec-

tiveness and appropriateness of care provided at the hospital, and sampling variations (the likelihood that the mortality observed in the study group truly represents the experience in the total population).⁵³ Statistical models for predicting mortality risk based on patient characteristics have been developed for use in a number of different clinical situations, including adult medical and intensive care, pediatric intensive care, and neonatal intensive care.^{54–58} These risk adjustment models can be used to compare the observed outcomes at a particular hospital with the outcomes that would be expected based on the demographic characteristics of the hospital's patients as well as the severity of their illnesses measured by physiologic and laboratory values. After differences in patient risk and sampling variations have been accounted for, residual variation in outcome is assumed to reflect differences in the effectiveness and/or appropriateness of medical care.

One of the earliest examples of risk adjustment for the evaluation of perinatal care was reported by Williams.³⁷ He applied a model for predicting neonatal death based on birth weight, race, sex, and multiple birth to more than 3 million infants born at 504 hospitals in California during the years 1960 to 1973. After the

correlated with other indicators of severity, including nursing workload, therapeutic intensity, and physician estimates of mortality risk. Furthermore, the SNAP increases the accuracy of neonatal mortality risk prediction when used along with birth weight, five-minute Apgar score, and size for gestational age.⁶⁰ In the future, use of scoring systems such as the SNAP will help to refine the risk adjustment analyses and provide us with a clearer picture of variations in neonatal mortality across hospitals.

The International Neonatal Network has developed the Clinical Risk Index for Babies (CRIB), a scoring system for predicting mortality risk for infants weighing 1,500 grams (3 pounds, 5 ounces) or less.⁶¹ The CRIB score is based on birth weight, gestational age, maximum and minimum fraction of inspired oxygen, maximum base excess, and presence of congenital malformations. The score uses values obtained within 12 hours of admission. The CRIB score is more accurate than birth weight alone in predicting mortality risk, and higher scores are associated with an increased risk for major cerebral abnormality.

Because postadmission data may reflect the results of treatments provided in the neonatal intensive care unit rather than the infants' underlying risk, mortality prediction models based only on admission data are preferred if the goal of risk adjustment is to identify differences in the effectiveness of care. Both the SNAP and the CRIB score use information collected during the first 12 to 24 hours after admission to the neonatal intensive care unit for predicting mortality risk.

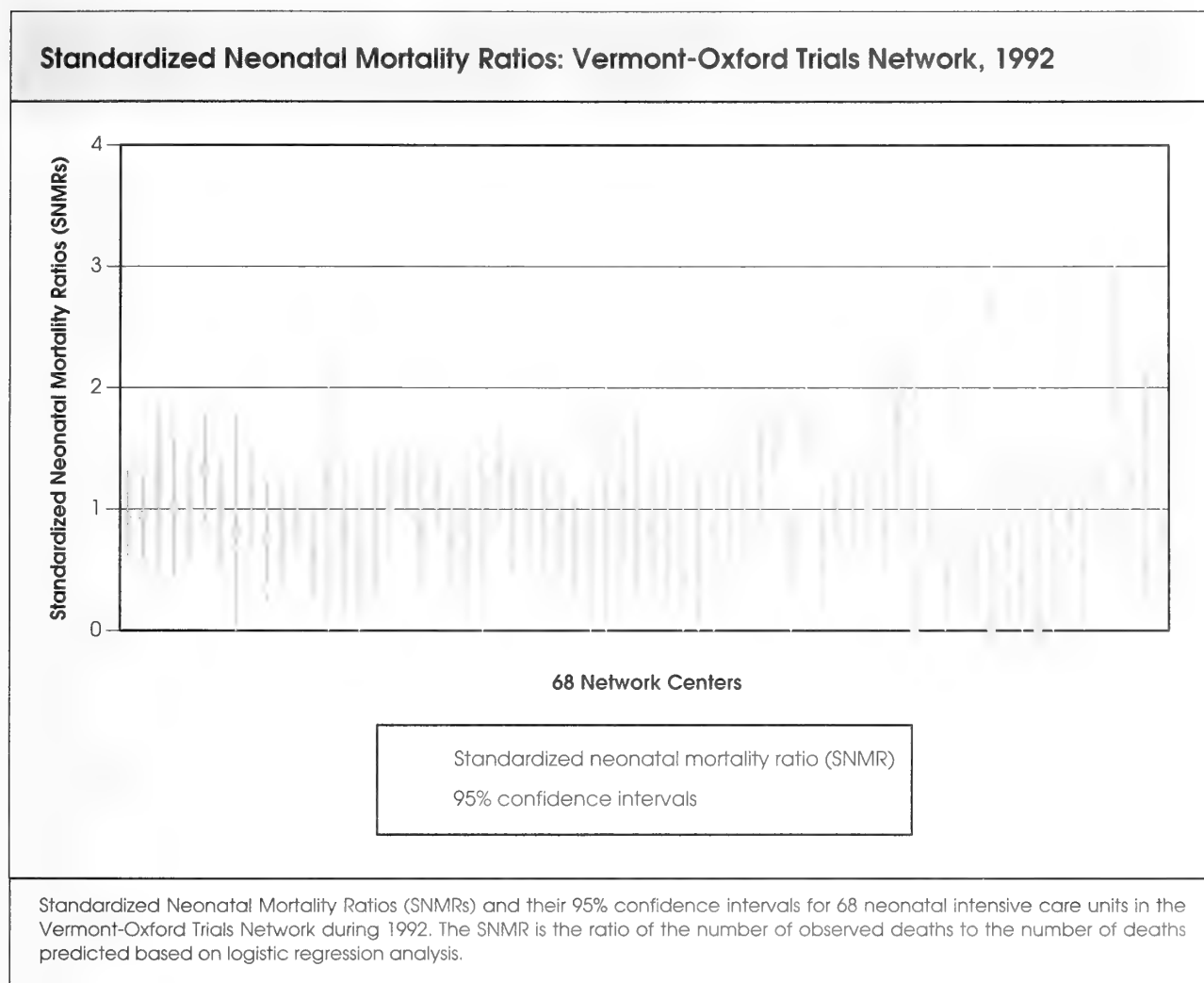
Figure 1 shows the standardized neonatal mortality ratios (SNMRs) at 68 centers participating in the Vermont-Oxford Trials Network in 1992, and illustrates the existing variation in mortality rates in these centers. In this model, which is based on factors present at the time of admission, the observed variations cannot be attributed to the infant's birth weight, race, gender, health at birth, receipt of prenatal care, and location of the birth because the effects of these factors have been statistically controlled. The SNMR is the ratio of the number of observed deaths at a center to the number of deaths predicted based on the patient characteristics in the model. An SNMR of 1 means that a hospital has exactly the number of deaths which would be expected; values greater than 1 indicate that more deaths occurred

Variations in the outcomes of hospitalized patients have been used as indicators of the effectiveness of medical care.

model had been used to account for newborn risk and the effect of chance, there was still a twofold variation in mortality at these hospitals. This residual unexplained variation was presumably the result of differences in the effectiveness of perinatal care.

More recently, risk adjustment models have been developed specifically for neonatal intensive care. Richardson and colleagues have developed the Score for Neonatal Acute Physiology (SNAP), which is patterned after the Acute Physiology and Chronic Health Evaluation (APACHE) score used in adult intensive care and the PSI used in pediatric intensive care.⁵⁹ The SNAP can be applied to all NICU admissions regardless of birth weight. The SNAP is predictive of neonatal mortality even within narrow birth weight strata and is

Figure 1



Source: *The Vermont-Oxford Trials Network 1992 Annual Report*. Burlington, VT: Neonatal Research and Technology Assessment, 1993.

than were expected; values less than 1 indicate that fewer deaths occurred than were expected. Although some hospitals have SNMRs that are less than 1 and others have SNMRs that are greater than 1, in most instances the 95% confidence limit includes the values of 1, which means that these hospitals do not appear to have too many or too few deaths. Improved predictor models which include major birth defects among the predictor variables are currently being developed.

Neonatal mortality prediction could serve several purposes. One purpose is the prediction of individual patient risk. It is unlikely that any model will be accurate enough to aid in patient care decisions such as when to withhold or withdraw life support. However, prediction of individual risk may be useful for identifying infants who died despite having a low pre-

dicted probability of death. These cases could then be chosen for audit as part of local quality improvement efforts.

A second purpose for neonatal risk prediction is the identification of outlier hospitals where the quality or effectiveness of care is low. Given the relatively small number of very low birth weight infants treated at individual neonatal intensive care units, the confidence intervals for estimates of measures like the SNMR will be large.⁶² This will severely limit the power of even very accurate statistical models to identify outlier hospitals. Aggregating cases over multiple years increases the ability to detect outliers. It remains to be proven, however, that targeting hospitals in this way accurately identifies units providing less effective care,⁶³ as methods to adjust for the underlying risks and differences in the units remain imperfect.

A third purpose for neonatal risk prediction models is their use in studies of hospital characteristics associated with outcome. The power to detect differences in risk-adjusted mortality rates among groups of hospitals within large neonatal networks will be greater than the power to detect individual outliers. Several studies have already shown that hospital characteristics are associated with outcomes for adult and neonatal patients.^{37,64} Williams, in the study discussed above, found that, after adjusting for patient risk, hospitals with larger delivery services, urban hospitals, hospitals performing above-average numbers of cesarean sections, those recording Apgar scores, and hospitals with higher specialist-to-generalist ratios had lower mortality rates.³⁷ Conversely hospitals with more Spanish-surnamed mothers and private proprietary hospitals had higher mortality rates. Paneth and colleagues have shown that risk-adjusted neonatal mortality rates at level 3 hospitals are

The gold standard for evaluating the efficacy of an intervention is the randomized controlled trial.

lower than at either level 1 or level 2 hospitals in New York City.^{15,16} The International Neonatal Network has also shown that mortality rates adjusted for risk using the CRIB score are lower in tertiary as opposed to nontertiary neonatal care units in the United Kingdom.⁵⁷

We are currently using data from the Vermont-Oxford Trials Network to investigate whether hospital characteristics, services, and staffing patterns are associated with differences in mortality for very low birth weight infants. It is not known whether patient volume, teaching status, hospital ownership, and use of ancillary personnel such as neonatal nurse practitioners influence the costs and outcomes of neonatal intensive care. Because of trends toward deregionalization of care and changing patterns of referrals due to managed care, it will be increasingly important to understand how these factors affect both costs and outcome. Neonatal networks will be valuable laboratories for answering health services questions about the delivery of neonatal intensive care.

Assessment of Interventions

Randomized Controlled Trials

The third step in the process for evaluating and improving the effectiveness of neonatal intensive care is assessing the efficacy of specific interventions. The gold standard for evaluating the efficacy of an intervention is the randomized controlled trial. The National Perinatal Epidemiology Unit in the United Kingdom has demonstrated how large, simple randomized controlled trials (RCTs) can be applied to answer important questions in perinatal medicine.⁶⁵ Most medical innovations lead to only small or moderate gains over standard treatment, but large trials are required to demonstrate such gains. For example, to have a reasonable chance of demonstrating that a new treatment reduces mortality from 25% to 20% requires a study that enrolls nearly 3,000 infants, many more infants than are generally admitted to any one NICU in a year. In the past, too many of the trials performed in neonatology were single-center studies enrolling relatively few patients. It is now clear that multicenter networks will be needed to perform the large trials required to demonstrate small, but clinically important, differences between treatments. The recent multicenter trials of surfactant therapy,⁶⁶ high-frequency ventilation,⁶⁷ and cryotherapy for retinopathy of prematurity⁶⁸ are examples of how this approach can be used successfully to test new therapies for neonatal intensive care.

A number of new therapies and technologies that are now in the early stages of clinical development will require multicenter randomized clinical trials to demonstrate their safety and efficacy for treatment of low birth weight infants (see Table 3).^{69–82} Several of these treatments have already been tested in initial small trials or are currently being evaluated in multicenter trials.

It is instructive to compare the situation in neonatology with that in pediatric oncology. Eighty to ninety percent of children in the United States with cancer are cared for at institutions participating in one of two national collaborative networks (Children's Cancer Study Group or Pediatric Oncology Group), using strictly defined treatment protocols.⁸³ These groups continually refine their treatment protocols based on the results of ongoing ran-

Table 3

New Therapies and Technologies that Require Evaluation for Use in Low Birth Weight Infants		
Therapy	Condition	Related Endnote Numbers
Erythropoietin	Anemia of prematurity	Shannon ⁶⁹
Vitamin A	Chronic lung disease	Shenai, Kennedy, Chytil, and Stahlman ⁷⁰
Inositol	Chronic lung disease	Hallman, Bry, Hoppu, et al. ⁷¹
Early corticosteroids	Chronic lung disease	Yeh, Torre, Rastogi, et al. ⁷²
Aerosolized corticosteroids	Chronic lung disease	La Force and Brudno ⁷³
Neuroprotective drugs	Ischemic brain injury	Traystman, Kirsch, and Koehler ⁷⁴
Metalloporphyrins	Hyperbilirubinemia	Valaes, Petmezaki, Henschke, et al. ⁷⁵
Oral immunoglobulin	Necrotizing enterocolitis	Eibi, Wolf, Furnkrantz, and Rosenbranz ⁷⁶
Developmental stimulation	Psychosocial development	Lester and Trunick ⁷⁷
Nitric oxide	Pulmonary hypertension	Abman, Kinsella, Shaffer, and Wilkening ⁷⁸
Extracorporeal membrane oxygenation (ECMO)	Respiratory failure	Revenis, Glass, and Short ⁷⁹
Liquid ventilation	Respiratory failure	Greenspan, Wolfson, Rubenstein, and Shaffer ⁸⁰
Patient-triggered ventilation	Respiratory failure	Bancalari ⁸¹
Supplemental oxygen	Retinopathy of prematurity	Phelps ⁸²

Sources: See the related endnote numbers at the end of this article for complete citations.

domized clinical trials. As a result, the outcomes for children with cancer have improved steadily.⁸⁴ We should strive for a similar organizational structure in neonatal intensive care.

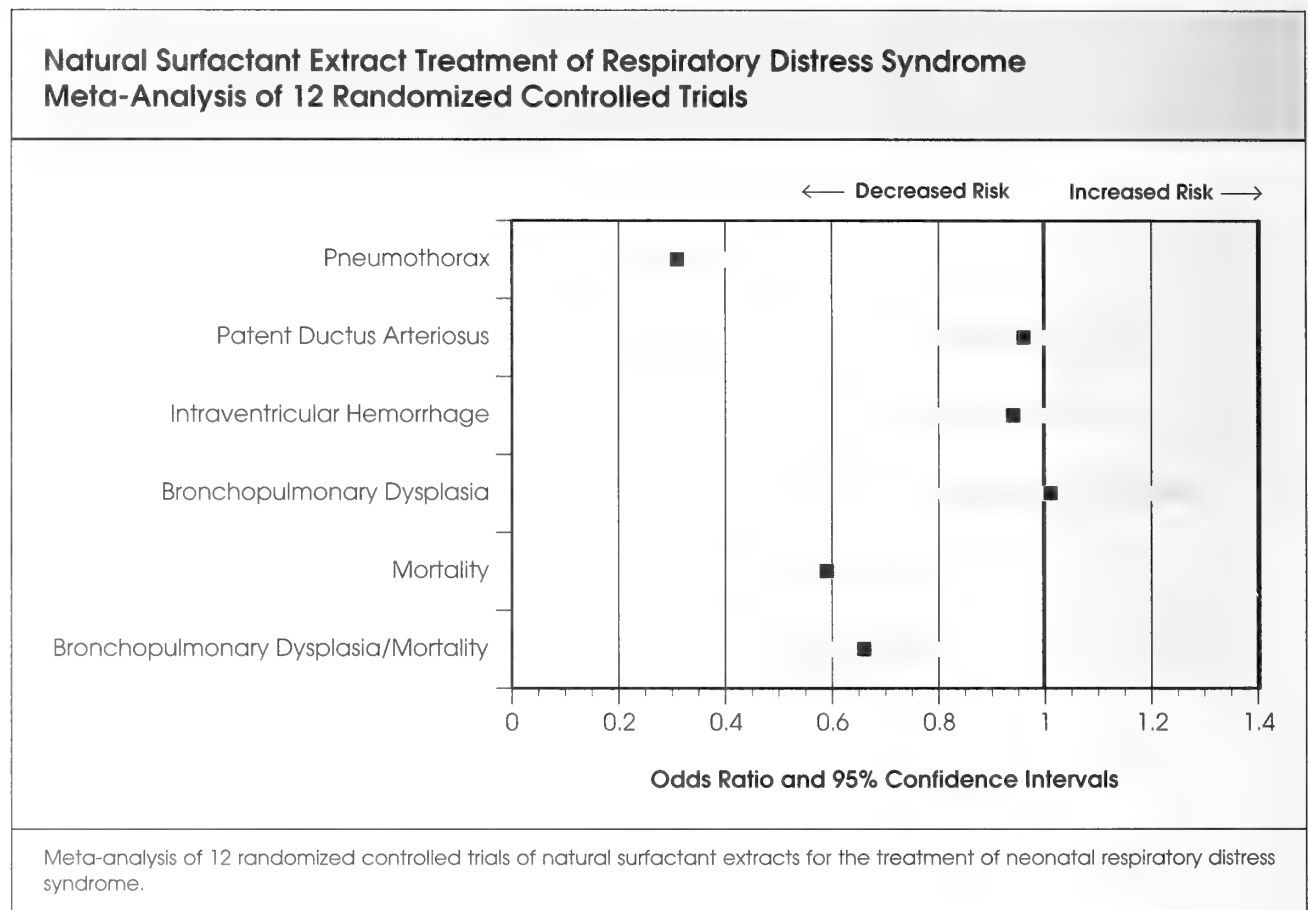
Despite a central role in evaluating neonatal technologies, randomized trials will not be capable of answering all of the questions that arise about interventions in neonatal intensive care.

Feinstein has pointed out that randomized controlled trials are not feasible for studying multiple therapeutic candidates, minor changes in therapy, instabilities caused by rapid technological improvements in available treatment, long-term adverse side effects, studies of etiologic or other suspected "noxious" agents, and the diverse clinical roles of diagnostic technology.⁸⁵ Additional methods will be required to address these issues. Observational studies based on large neonatal data bases from multicenter networks will have a role in addressing those questions that cannot readily be answered using randomized trials.

Meta-Analysis: Combining Data from Many Randomized Trials

The evaluation of specific interventions requires a synthesis of all the available evidence. Traditionally, such a synthesis took the form of a qualitative literature review. Recently, statistical techniques for combining the findings of individual studies have come into widespread use. The formal overview, or meta-analysis, arrives at a summary measure of effect size by combining the results of individual trials.⁸⁶ Meta-analysis provides a powerful tool for evaluating the evidence from randomized controlled trials. However, investigators must approach meta-analysis with the same methodologic rigor as any other research. Overviews should include all relevant trials which meet predefined inclusion criteria. The results of the trials are extracted from published reports and, in some instances, supplemented with unpublished data obtained from the investigators. These results are then tabulated, and summary measures of effect size are calculated. Several different statistical

Figure 2



Source: Mercier, C.E., and Soll, R.F. Clinical trials of natural surfactant extract in respiratory distress syndrome. *Clinics in Perinatology* (1993) 20:723-25.

methods for determining the summary measures are available.⁸⁷

The method of meta-analysis has been extensively applied to synthesizing the results of randomized trials in perinatal medicine. Formal meta-analyses, or overviews, have been included in the *Oxford Database of Perinatal Trials*, which contains a bibliography of all randomized trials in prenatal medicine published since 1940.^{88,89} Several obstetrical overviews⁹⁰ and neonatal overviews have also been published.⁹¹

These reference works will be updated and published in electronic format, providing extensive statistical summaries of the available evidence for perinatal interventions. The highly respected Cochrane Collaboration has been established to coordinate and disseminate overviews of randomized trials which can be used to inform evidence-based decision making.

An example of a recent meta-analysis is the overview by Mercier and Soll of the effects of natural surfactant therapy for the

treatment of respiratory distress syndrome (see Figure 2).⁹² This overview is based on 12 separate randomized trials. Taken together, these trials indicate that surfactant therapy reduces the risks for serious lung diseases and mortality.

The individual trials did not each demonstrate these results. Only by pooling the evidence from all of the trials do such clear conclusions emerge. Formal overviews such as this one are powerful tools for evaluating the efficacy and safety of specific interventions.

A novel form of meta-analysis has recently been described for combining the results of randomized trials and medical practice data bases. This method—called cross-design synthesis—identifies studies conducted using similar research designs, assesses the potential biases associated with each design, makes secondary adjustments of study results to correct for known biases, and develops models for synthesizing results which minimize hidden biases.⁹³ This untested method may prove

useful in the future because it combines the strengths of randomized trials for producing unbiased comparisons with the ability of patient data bases to include a broad range of patients treated in real-world conditions.

Economic Evaluation

Faced with limited reserves and the need to choose among alternative programs, policymakers must consider not only whether neonatal intensive care is effective but also whether it is worth the cost. Increasingly, analysts have come to rely on cost-effectiveness analyses to evaluate medical care and interventions.⁹⁴ In cost-effectiveness analyses, an estimate is made of the incremental costs of an improvement in health status (such as the cost of an additional year of life), attributable to a particular intervention and compared with the incremental costs of other interventions.

Cost-effectiveness analysis was one technique used in the most comprehensive economic evaluation of neonatal intensive care which was based on patients receiving intensive care in Hamilton-Wentworth County, Ontario, between 1973 and 1977.⁹⁵ In addition to measuring all of the costs flowing from neonatal intensive care, such as health care and special services received by survivors after discharge, the study attempted to measure the condition of survivors based on physical function, role function, social and emotional function, and health problems. These outcome data were used to adjust life years gained by NICU survivors by a factor that takes into account the quality of life for those who survived with disabilities. The resulting units are called quality-adjusted life-years (QALYs). For infants weighing from 1,000 to 1,499 grams (between 2 pounds, 3 ounces and 3 pounds, 5 ounces), the cost (in 1978 Canadian dollars) was \$59,500 per additional survivor, \$2,900 per life-year gained, and \$3,200 per QALY gained. For infants weighing from 500 to 999 grams (between 1 pound, 2 ounces and 2 pounds, 3 ounces), the costs were \$102,500 per additional survivor, \$9,300 per life-year gained, and \$22,400 per QALY gained.

These cost-effectiveness ratios have little intrinsic meaning by themselves but can be compared with ratios for other major health interventions. Figure 3 shows the cost per QALY, adjusted to 1986 U.S. dollars, for neonatal intensive care in the

two birth weight groups and for other selected health care interventions.⁹⁶ Several interventions—including coronary bypass surgery for single-vessel disease, school tuberculin testing, continuous ambulatory peritoneal dialysis, hospital hemodialysis, and liver transplantation—all have higher estimated costs per QALY gained than neonatal intensive care for infants weighing from 500 to 999 grams (between 1 pound, 2 ounces and 2 pounds, 3 ounces). For example, a liver transplant costs \$250,000 for each QALY gained while NICU care for a moderately low birth weight infant costs less than \$10,000 for each QALY.

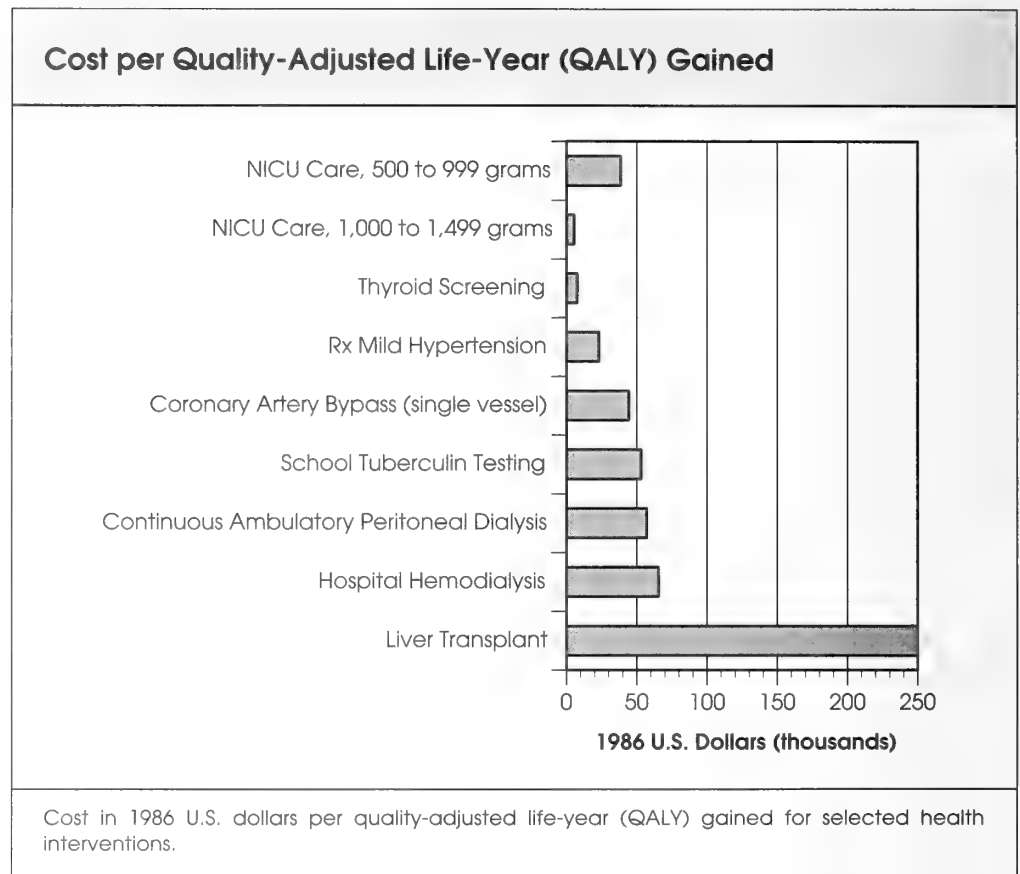
The Office of Technology Assessment, in its 1987 evaluation of neonatal intensive care, concluded: "Neonatal intensive care results in both increased survival and increased costs. Moreover, neonatal intensive care becomes more expensive as it is employed in increasingly marginal cases. The worth of a life saved, however, is ultimately a value judgment involving ethical and social considerations. The results from cost-effectiveness studies alone cannot guide decisions regarding who should receive care."²¹

These conclusions are still valid today. In addition, advances in neonatal intensive care have influenced both the costs and the outcomes of this care. Since the Canadian study was done, survival rates for infants weighing less than 1,000 grams (2 pounds, 3 ounces) have increased. A recent report from the province of Alberta, Canada, suggests that the condition of NICU survivors may also be improving.⁹⁷

Policymakers must consider not only whether neonatal intensive care is effective but also whether it is worth the cost.

The introduction of surfactant therapy has changed both outcomes and costs.^{12,13} It is estimated that use of surfactant among very low birth weight infants has resulted in a 30% decrease in mortality and a similar decrease in use of hospital resources.¹³ Several other investigators have concluded that surfactant therapy is cost-effective, but definitive analyses are still required.^{13,98-103} An economic evaluation of neonatal intensive care based on patients treated in the 1990s is urgently needed.

Figure 3



Source: Detsky, A.S. Are clinical trials a cost-effective investment? *Journal of the American Medical Association* (1989) 262:1795-1800.

Ultimately policymakers and society will have to decide whether resources should be allocated to neonatal intensive care as opposed to other purposes. Joyce and colleagues put this choice into perspective by comparing the cost-effectiveness of different strategies to reduce infant mortality.¹⁰⁴ They estimated that, if there was a direct causal relationship between prenatal care and infant mortality, it would cost between \$30 and \$40 (1984 U.S. dollars) to save an additional life by expanding the number of women who receive prenatal care in the first trimester, as opposed to \$2,000 or \$3,000 to save an additional life by expanding the number of low birth weight infants who receive neonatal intensive care.

Unfortunately, there is growing evidence that providing access to quality prenatal care alone is insufficient to reduce low birth weight. (See the article by Alexander and Korenbrot in this journal issue.)

Changing Physician Behavior

The final step in the process of evaluating and improving the effectiveness and efficiency of neonatal intensive care involves changing physicians' practices. Greco and Eisenberg have recently reviewed the general methods that can be used to alter the practice behavior of physicians.¹⁰⁵ These include (1) educational processes such as continuing medical education and practice guidelines, (2) feedback of information comparing individual physician practices and patient outcomes with benchmark standards, (3) continuous quality improvement programs and other efforts to engage physicians in change, (4) administrative interventions, and (5) financial incentives or penalties. In general, whether an intervention is successful depends on the particular circumstances in which it is used; combinations of methods appear to be the most effective.

Neonatal networks have the potential to influence practice patterns of neonatologists using several of these approaches. Membership in a data base that produces benchmarking reports, participation in meetings, communication with other network members, and the use of standardized research protocols supplies many elements needed to change neonatologists' behavior.

Participation in multicenter randomized clinical trials may itself be an educational process capable of causing changes in practice. Surfactant therapy for neonatal respiratory distress syndrome was rapidly adopted in nearly all neonatal intensive care units in North America soon after surfactants were commercially released in 1991. The strength of the experimental evidence and advertising by commercial sponsors were partly responsible for the rapid acceptance of surfactant therapy. The fact that hundreds of neonatal units actually participated in the randomized controlled trials conducted in the preceding decade also played a role.

Information from neonatal network data bases has the potential to influence physician behavior and neonatal intensive care practices.^{106,107} The Vermont-Oxford Trials Network currently provides members with reports containing feedback on how local practices and outcomes compare with those of the total network. These reports are intended for use in continuous quality improvement programs. The reports include data on risk-adjusted mortality, length of hospital stay, and adverse outcomes such as intraventricular hemorrhage (bleeding in the brain), chronic lung disease, necrotizing enterocolitis (severe damage to the intestines), nosocomial infection (infections acquired in the hospital), and retinopathy of prematurity (impaired vision or blindness). It will be important to evaluate how these reports are actually used by the members of the network and to determine whether such feedback leads to changes in physician behavior and improvements in the quality of neonatal intensive care.

The Role of Parents in Evaluating Neonatal Intensive Care

Parents and families must play a critical role in evaluating neonatal intensive care. Assessments of the benefits and costs of neonatal intensive care should incorporate the views and experiences of a broad range of families whose infants received

intensive care. A recent conference attended by neonatologists and parents who had personal experience with neonatal intensive care developed a set of "Principles for Family-Centered Neonatal Care," which will help parents and professionals work together.¹⁰⁸ Two of these principles focus directly on issues relating to the evaluation of neonatal intensive care. One principle urges that new treatments be introduced only in the context of properly controlled trials and states, "Experienced parents should have a voice in determining the research agenda, in establishing outcomes of interest, and in educating other parents about the need for ethically and scientifically sound research in neonatology." The other principle states, "Par-

"Parents and professionals must work together to promote meaningful long-term follow-up for all high risk NICU survivors."

ents and professionals must work together to promote meaningful long-term follow-up for all high risk NICU survivors."

Only a small percentage of infants receiving neonatal intensive care are currently enrolled in formal follow-up studies, and there are many unanswered questions about the quality of life, particularly for extremely low birth weight survivors.^{109,110} Those follow-up data that are available concentrate primarily on defining the incidence of neurologic deficits. A more complete evaluation of societal and familial costs and benefits is needed which takes into account the experience and opinions of parents and families and examines a broad range of health outcomes.¹¹¹ An evaluation of this kind will require collaboration between professionals and the parents and families whose infants have been cared for in neonatal intensive care units.

There is great interest in developing simple report cards by which patients can compare or judge results of various therapies. The New York State Department of Health is a leader in this field. Since 1991, it has supplied data to the public ranking cardiac surgical services and individual surgeons.¹¹² Other states have begun publishing similar data. This movement is bound to spread to neonatology. Com-

parative data will be of little value, however, unless they are carefully gathered and reported by a neutral source in a format that parents can understand. Neonatal networks will be capable of compiling the necessary data. Creative new ideas for presenting information, such as the use of interactive video disks, may help to explain the information to parents.

Conclusion

Nearly 15 years ago, Sinclair and colleagues concluded that, although the efficacy of specific neonatal intensive care interventions had been demonstrated, the overall effectiveness and efficiency of neonatal intensive care programs required validation in randomized controlled trials.⁷ Such trials have not yet been done. It is unlikely that they will be for several reasons. First, there is widespread agreement that neonatal intensive care saves lives. Second, there is considerable disagree-

ment about what to include in a standard package of neonatal intensive care given the multitude of elements that make up modern intensive care and the marked variations in practice which currently exist. Third, diagnostic and therapeutic technologies are changing so rapidly that any package of services would quickly become obsolete as new tests and treatments were introduced. Although the randomized controlled trial will remain the gold standard by which all new therapies must be judged, a broader range of methods drawn from clinical evaluation science will be needed if the effectiveness of neonatal intensive care as a whole is to be monitored and continuously improved. The proper question is no longer "Does neonatal intensive care work?" but rather "How can neonatal intensive care be made more effective and efficient?" Neonatal research networks will play an important role in finding the answers and applying them.

1. National Committee on Perinatal Health. *Toward improving the outcome of pregnancy*. White Plains, NY: National Foundation–March of Dimes, 1976.
2. McCormick, M.C., Shapiro, S., and Starfield, B.H. The regionalization of perinatal services: Summary of the evaluation of a national demonstration program. *Journal of the American Medical Association* (1985) 253:799–804.
3. Butterfield, L.J. Organization of regional perinatal programs. *Seminars in Perinatology* (1977) 1:217–33.
4. American Hospital Association. *Hospital statistics*. Chicago: AHA, 1989.
5. Merenstein, G.B., Rhodes, P.G., and Little, G.A. Personnel in neonatal pediatrics: Assessment of numbers and distribution. *Pediatrics* (1985) 76:454–56.
6. Silverman, W.A. Is neonatal medicine in the United States out of step? *Pediatrics* (1993) 92:612–13.
7. Sinclair, J.C., Torrance, G.W., Boyle, M.H., et al. Evaluation of neonatal-intensive care programs. *New England Journal of Medicine* (1981) 305:489–94.
8. Lee, K.S., Paneth, N., Gartner, L.M., et al. Neonatal mortality: An analysis of the recent improvement in the United States. *American Journal of Public Health* (1980) 70:15–21.
9. Williams, R.L., and Chen, P.M. Identifying the sources of the recent decline in perinatal mortality rates in California. *New England Journal of Medicine* (1982) 306:207–14.
10. Buehler, J.W., Kleinman, J.C., Hogue, C.J.R., et al. Birth weight-specific infant mortality, United States, 1960 and 1980. *Public Health Reports* (1987) 102:151–61.
11. Hiltz, P.J. U.S. reports drop in infant deaths. *New York Times*. April 6, 1991, at A1.
12. Horbar, J.D., Wright, E.C., Onstad, L., et al. Decreasing mortality associated with the introduction of surfactant therapy: An observational study of neonates weighing 601 to 1300 grams at birth. *Pediatrics* (1993) 92:191–96.
13. Schwartz, R.M., Luby, A.M., Scanlon, J.W., and Kellogg, R.J. Effect of surfactant on morbidity, mortality, and resource use in newborn infants weighing 500 to 1500 g. *New England Journal of Medicine* (1994) 30:1476–80.
14. Paneth, N. Technology at birth. Editorial. *American Journal of Public Health* (1990) 80:791–92.

15. Paneth, N., Kiely, J., Wallenstein, S., and Susser, M. The choice of place of delivery: Effect of hospital level on mortality in all singleton births in New York City. *American Journal of Diseases of Childhood* (1987) 141:60–64.
16. Paneth, N., Kiely, J.L., Wallenstein, S., et al. Newborn intensive care and neonatal mortality in low-birth-weight infants: A population study. *New England Journal of Medicine* (1982) 307:148–55.
17. Gortmaker, S., Sobol, A., Clark, C., et al. The survival of very low-birth weight infants by level of hospital at birth: A population study of perinatal systems in four states. *American Journal of Obstetrics and Gynecology* (1985) 152:517–24.
18. Mayfield, J.A., Rosenblatt, R.A., Baldwin, L.M., et al. The relation of obstetrical volume and nursery level to perinatal mortality. *American Journal of Public Health* (1990) 80:819–23.
19. Verloove-Vanhorick, S.P., Verwey, R.A., Ebeling, M.C.A., et al. Mortality in very preterm and very low birthweight infants according to place of birth and level of care: Results of a national collaborative survey of preterm and very low birthweight infants in the Netherlands. *Pediatrics* (1988) 81:404–11.
20. Horwood, S.P., Boyle, M.H., Torrance, G.W., and Sinclair, J.C. Mortality and morbidity of 500- to 1,499-gram birth weight infants live-born to residents of a defined geographic region before and after neonatal intensive care. *Pediatrics* (1982) 69:5613–20.
21. U.S. Congress, Office of Technology Assessment. *Neonatal intensive care for low birthweight infants: Costs and effectiveness*. Health Technology Case Study 38. OTA-HCS-38. Washington, DC: OTA, 1987.
22. Bhushan, V., Paneth, N., and Kiely, J.L. Impact of improved survival of very low birth weight infants on recent secular trends in the prevalence of cerebral palsy. *Pediatrics* (1993) 91:1094–1100.
23. McCormick, M.C. The contribution of low birth weight to infant mortality and childhood morbidity. *New England Journal of Medicine* (1985) 312:82–90.
24. McCormick, M.C. Long-term follow-up of infants discharged from neonatal intensive care units. *Journal of the American Medical Association* (1989) 261:1767–72.
25. McCormick, M.C., Brooks-Gunn, J., Workman-Daniels, K., et al. The health and developmental status of very low-birth-weight children at school age. *Journal of the American Medical Association* (1992) 267:2204–8.
26. Hack, M., Taylor, G., Klein, N., et al. School-age outcomes in children with birth weights under 750g. *New England Journal of Medicine* (1994) 331:753–59.
27. Saigal, S., Rosenbaum, P., and Stoskopf, B. Comprehensive assessment of the health status of extremely low birth weight children at eight years of age: Comparison with a reference group. *Journal of Pediatrics* (1994) 125:411–17.
28. Shankaran, S., Cohen, S.N., Linver, M., and Zonia, S. Medical care costs of high-risk infants after neonatal intensive care: A controlled study. *Pediatrics* (1988) 81:372–78.
29. McCormick, M.C., Bernbaum, J.C., Eisenberg, J.M., et al. Costs incurred by parents of very low birth weight infants after the initial neonatal hospitalization. *Pediatrics* (1991) 88:533–41.
30. Hack, M., and Fanaroff, A. Outcomes of extremely-low-birth-weight infants between 1982 and 1988. *New England Journal of Medicine* (1989) 321:1642–47.
31. Allen, M.C., Donohue, P.K., and Dusman, A.E. The limit of viability—Neonatal outcome of infants born at 22 to 25 weeks' gestation. *New England Journal of Medicine* (1993) 329:1597–601.
32. Nishida, H., and Ishizuka, M.E. Survival rate of extremely low birthweight infants and its effect on the amendment of the Eugenic Protection Act in Japan. *Acta Paediatrica Japonica* (1992) 34:612–16.
33. Nishida, H. The viability limit of gestation for the fetus and premature neonates. *Asian Medical Journal* (1992) 35:487–94.

34. Aday, L.A., Begley, C.E., Lavison, D.R., and Slater, C.H. *Evaluating the medical care system: Effectiveness, efficiency and equity*. Ann Arbor, MI: Health Administration Press, 1993.
35. Raskin, I.E., and Maklau, C.W. Medical treatment effectiveness research: A view from inside the Agency for Health Care Policy and Research. *Evaluation and the Health Professions* (1991) 14:161–86.
36. Roper, W.L., Winkenwerder, W., Hackbarth, G.M., and Krakauer, H. Effectiveness in health care: An initiative to evaluate and improve medical practice. *New England Journal of Medicine* (1988) 319:1197–1202.
37. Williams, R.L. Measuring the effectiveness of perinatal medical care. *Medical Care* (1979) 17:95–110.
38. National Committee on Perinatal Health. *Toward improving the outcome of pregnancy: The 90s and beyond*. White Plains, NY: March of Dimes Birth Defects Foundation, 1993.
39. Investigators of the Vermont-Oxford Trials Network Database Project. The Vermont-Oxford Trials Network: Very low birth weight outcomes for 1990. *Pediatrics* (1993) 91:540–45.
40. Hack, M., Horbar, J.D., Malloy, M.H., et al. Very low birth weight outcomes of the National Institute of Child Health and Human Development Neonatal Network. *Pediatrics* (1991) 87:587–97.
41. The Vermont-Oxford Trials Network. A multicenter randomized trial comparing synthetic surfactant to modified bovine surfactant extract in the treatment of neonatal respiratory distress syndrome. *Pediatric Research* (1994) 35:259A.
42. Fanaroff, A., Wright, E., Korones, S., et al. A controlled trial of phophylactic intravenous immunoglobulin (IVIG) to reduce noscomical infections in VLBW infants. *New England Journal of Medicine* (1994) 330:1107–13.
43. Horbar, J.D., Wright, L.L., and Soll, R.F. A multicenter randomized trial comparing two surfactants for the treatment of neonatal respiratory distress syndrome. *Journal of Pediatrics* (1993) 123:757–66.
44. Wennberg, J., and Gittlesohn, A. Small area variations in health care delivery. *Science* (1973) 182:1102–8.
45. Health Care Financing Administration. *Medicare hospital information 1988, 1989, 1990*. Vol. 55. Technical supplement. Washington, DC: U.S. Department of Health and Human Services, 1992.
46. Ballard, P.L. Glucocorticoid effects in vivo. In *Monographs in endocrinology*. Vol. 28: Hormones and lung maturation. P.L. Ballard, ed. Berlin: Springer-Verlag, 1986, pp. 24–71.
47. Crowley, P. Promoting pulmonary maturity. In *Effective care in pregnancy and childbirth*. I. Chalmers, M. Enkin, M. Keirse, eds. Oxford: Oxford University Press, 1989, pp. 746–64.
48. Horbar, J.D. *Antenatal corticosteroid administration and neonatal outcomes for infants 501 to 1500 grams: Vermont-Oxford Trials Network 1991–1992*. Program and abstracts of the NIH Consensus Development Conference on the Effect of Corticosteroids for Fetal Maturation on Perinatal Outcomes. Bethesda, MD: National Institute of Health, 1994, pp. 47–52.
49. *The Vermont-Oxford Trials Network 1992 Annual Report*. Burlington, VT: Neonatal Research and Technology Assessment, 1993.
50. Avery, M.E., Tooley, W.H., and Keller, J.B. Is chronic lung disease in low birth weight infants preventable? A survey of eight centers. *Pediatrics* (1987) 79:26–30.
51. Horbar, J.D., McAuliffe, T.L., and Adler, S.M. Variability in 28-day outcomes for very low birth weight infants: An analysis of 11 neonatal intensive care units. *Pediatrics* (1988) 82:554–59.
52. Kraybill, E.N., Bose, C.L., and D'Ercole, A.J. Chronic lung disease in infants with very-low-birthweight: A population based study. *American Journal of Diseases of Children* (1987) 141:784–88.
53. Jencks, S.F., Daley, J., Draper, D., et al. Interpreting hospital mortality data: The role of clinical risk adjustment. *Journal of the American Medical Association* (1988) 260:3611–16.

54. Hadorn, D.C., Keeler, E.B., Rogers, W.H., and Brook, R.H. *Assessing the performance of mortality prediction models*. Santa Monica, CA: RAND, 1993.
55. Pollack, M.M., Ruttiman, U.E., Getson, P.R., et al. Accurate prediction of the outcome of pediatric intensive care: A new quantitative method. *New England Journal of Medicine* (1987) 316:134–39.
56. Richardson, D.K., Gray, J.E., McCormick, M.C., et al. Score for neonatal acute physiology: A physiologic severity index for neonatal intensive care. *Pediatrics* (1993) 91:617–23.
57. International Neonatal Network. The CRIB (clinical risk index for babies) score: A tool for assessing initial neonatal risk and comparing performance of neonatal intensive care units. *Lancet* (1993) 342:193–98.
58. Horbar, J.D., Onstad, L., Wright, E., et al. Predicting mortality risk for infants weighing 501 to 1500 grams at birth: A National Institutes of Health Neonatal Research Network report. *Critical Care Medicine* (1993) 21:12–18.
59. Richardson, D.K., Gray, J.E., McCormick, M.C., et al. Score for neonatal acute physiology: A physiologic severity index for neonatal intensive care. *Pediatrics* (1993) 91:617–23.
60. Richardson, D.K., Phibbs, C.S., Gray, J.E., et al. Birth weight and illness severity: Independent predictors of neonatal mortality. *Pediatrics* (1993) 91:969–75.
61. See note no. 57, International Neonatal Network, for more information about the CRIB score.
62. Horbar, J.D. Birthweight-adjusted mortality rates for assessing the effectiveness of neonatal intensive care. *Medical Decision Making* (1992) 12:259–64.
63. Park, R.E., Brook, R.H., and Kosecoff, J. Explaining variations in hospital death rates. *Journal of the American Medical Association* (1990) 264:484–90.
64. Hartz, A.J., Krakauer, H., Kuhn, E.M., et al. Hospital characteristics and mortality rates. *New England Journal of Medicine* (1989) 321:1720–25.
65. National Perinatal Epidemiology Unit 1991 Report. Oxford: National Perinatal Epidemiology Unit, 1992.
66. Soll, R.F., and McQueen, M.C. Respiratory distress syndrome. In *Effective care of the newborn infant*. J.C. Sinclair and M.B. Bracken, eds. Oxford: Oxford University Press, 1992, pp. 325–55.
67. HIFI Study Group. High-frequency oscillatory ventilation compared with conventional mechanical ventilation in the treatment of respiratory failure in preterm infants. *New England Journal of Medicine* (January 12, 1989) 320:88–93.
68. Cryotherapy for Retinopathy of Prematurity Cooperative Group. Multicenter trial of cryotherapy for retinopathy of prematurity: Preliminary results. *Pediatrics* (1988) 81:697–706.
69. Shannon, K. Recombinant erythropoietin in anemia of prematurity: Five years later. *Pediatrics* (1993) 92:614–16.
70. Shenai, J.P., Kennedy, K.A., Chytil, F., and Stahlman, M.T. Clinical trial of vitamin A supplementation in infants susceptible to bronchopulmonary dysplasia. *Journal of Pediatrics* (1987) 111:269–77.
71. Hallman, M., Bry, K., Hoppu, K., et al. Inositol supplementation in premature infants with respiratory distress syndrome. *New England Journal of Medicine* (1992) 326:1233–39.
72. Yeh, T.F., Torre, J.A., Rastogi, A., et al. Early postnatal dexamethasone therapy in premature infants with severe respiratory distress syndrome: A double-blind, controlled study. *Journal of Pediatrics* (1990) 117:273–82.
73. La Force, W.R., and Brudno, S. Controlled trials of beclomethasone dipropionate by nebulization in oxygen and ventilator-dependent infants. *Journal of Pediatrics* (1993) 122:285–88.
74. Traystman, R.J., Kirsch, J.R., and Koehler, R.C. Oxygen radical mechanisms of brain injury following ischemia and reperfusion. *Journal of Applied Physiology* (1991) 71:1185–95.
75. Valaes, T., Petmezaki, S., Henschke, C., et al. Control of jaundice in preterm newborns by an inhibitor of bilirubin production: Studies with tin-mesoporphyrin. *Pediatrics* (1994) 93:1–11.

76. Eibi, M.M., Wolf, H.M., Furnkrantz, H., and Rosenbranz, A. Prevention of necrotizing enterocolitis in low-birth-weight infants by IgA-IgG feeding. *New England Journal of Medicine* (1988) 319:1-7.
77. Lester, B.M., Trunick, E.Z. Introduction: Guidelines for stimulation with preterm infants. *Clinics in Perinatology* (1990) 17:xv-xvii.
78. Abman, S.H., Kinsella, J.P., Shaffer, M.S., and Wilkening, R.B. Inhaled nitric oxide in the management of a premature newborn with severe respiratory distress and pulmonary hypertension. *Pediatrics* (1993) 92:606-9.
79. Revenis, M.E., Glass, P., and Short, B.L. Mortality and morbidity rates among lower birth weight infants (2000 to 2500 grams) treated with extracorporeal membrane oxygenation. *Journal of Pediatrics* (1992) 121:452-58.
80. Greenspan, J.S., Wolfson, M.R., Rubenstein, S.D., and Shaffer, T.H. Liquid ventilation of human preterm neonates. *Journal of Pediatrics* (1990) 117:106-11.
81. Bancalari, E. *Mechanical ventilation—New strategies*. Program/Syllabus Hot Topics '93 in Neonatology. Columbus, OH: Ross Laboratories, 1993, pp. 119-32.
82. Phelps, D.L. Retinopathy of prematurity. *Current Problems in Pediatrics* (September 1992) 22,8:349-71.
83. Bleyer, W.A. The impact of childhood cancer in the United States and the world. *CA: A Cancer Journal for Clinicians* (1990) 40:355-67.
84. Kramer, S., Meadows, A.T., Pastore, G., et al. Influence of place of treatment on diagnosis, treatment, and survival in three pediatric solid tumors. *Journal of Clinical Oncology* (1984) 2:917-23.
85. Feinstein, A.R. An additional basic science for clinical medicine: IV. The development of clinimetrics. *Annals of Internal Medicine* (1983) 99:843-48.
86. Sacks, H.S., Berrier, J., Reitman, D., et al. Meta-analyses of randomized controlled trials. *New England Journal of Medicine* (1987) 316:450-55.
87. Bracken, M.B. Statistical methods for analysis of effects of treatment on overviews of randomized trials. In *Effective care of the newborn infant*. J.C. Sinclair and M.B. Bracken, eds. Oxford: Oxford University Press, 1992, pp. 13-18.
88. *A classified bibliography of controlled trials in perinatal medicine, 1940-1984*. Oxford: Oxford University Press, 1985.
89. Chalmers, I. *Oxford database of perinatal trials*. Version 1.2, Spring 1992 disk issue 7. Oxford: Oxford University Press, 1992.
90. Chalmers, I., Enkin, M., and Keirse, M., eds. *Effective care in pregnancy and childbirth*. Vols. 1 and 2. Oxford: Oxford University Press, 1989.
91. Sinclair, J.C., and Bracken, M.B., eds. *Effective care of the newborn infant*. Oxford: Oxford University Press, 1992.
92. Mercier, C.E., and Soll, R.F. Clinical trials of natural surfactant extract in respiratory distress syndrome. *Clinics in Perinatology* (1993) 20:711-35.
93. Korper, S., Mosteller, F., and Weissman, N. Cross-design synthesis: A new form of meta-analysis for combining results from randomized clinical trials and medical-practice databases. *International Journal of Technology Assessment in Health Care* (1993) 9:440-49.
94. Racine, A.D., Joyce, T.J., and Grossman, M. Effectiveness of health services for pregnant women and infants. *The Future of Children* (Winter 1992) 2,2:40-57.
95. Boyle, M.H., Torrance, G.W., Sinclair, J.C., and Horwood, S.P. Economic evaluation of neonatal intensive care of very-low-birth-weight infants. *New England Journal of Medicine* (1983) 308:1330-37.
96. Detsky, A.S. Are clinical trials a cost-effective investment? *Journal of the American Medical Association* (1989) 262:1795-1800.
97. Robertson, C., Sauve, R.S., and Christianson, H.E. Province-based study of neurologic disability among survivors weighing 500 through 1249 grams at birth. *Pediatrics* (1994) 93:636-40.
98. Mugford, M., Piercy, J., and Chalmers, I. Cost implications of different approaches to the prevention of respiratory distress syndrome. *Archives of Diseases of Childhood* (1991) 66:757-64.
99. Maniscalco, W.M., Kendig, J.W., and Shapiro, D.L. Surfactant replacement therapy: Impact on hospital charges for premature infants with respiratory distress syndrome. *Pediatrics* (1989) 83:1-6.

100. Tubman, T.R.J., Halliday, H.L., and Normand, C. Cost of surfactant replacement treatment for severe neonatal respiratory distress syndrome: A randomised controlled trial. *British Medical Journal* (1990) 301:842-45.
101. Egberts, J. Estimated costs of different treatments of the respiratory distress syndrome in a large cohort of preterm infants of less than 30 weeks of gestation. *Biology of the Neonate* (1992) 61 (suppl. 1):59-65.
102. Merritt, T.A., Hallman, M., Vaucher, Y., et al. Impact of surfactant treatment on cost of neonatal intensive care: A cost benefit analysis. *Journal of Perinatology* (1990) 10:416-19.
103. Soll, R.F., Jacobs, J., Pashko, S., and Thomas, R. Cost effectiveness of beractant in the prevention of respiratory distress syndrome. *Pharmacoeconomics* (1993) 4:278-86.
104. Joyce, T., Corman, H., and Grossman, M. A cost-effectiveness analysis of strategies to reduce infant mortality. *Medical Care* (1988) 26:348-60.
105. Greco, P.J., and Eisenberg, J.M. Changing physicians' practices. *New England Journal of Medicine* (1993) 329:1271-74.
106. Wirtschafter, D.D., Jones, K.R., and Thomas, J.T. Using health care outcomes to improve patient care in the NICU. *Journal of Quality Improvement* (1994) 10:57-65.
107. Holthof, B., and Prins, P. Comparing hospital perinatal mortality rates: A quality improvement instrument. *Medical Care* (1993) 31:801-7.
108. Harrison, H. The principles for family-centered neonatal care. *Pediatrics* (1993) 92:643-50.
109. McCormick, M.C. Has the prevalence of handicapped infants increased with improved survival of the very low birth weight infant? *Clinics in Perinatology* (1993) 20:263-77.
110. Robertson, M.R.C. Should we look after babies less than 800 grams? *Archives of Diseases of Childhood* (1993) 68:326-29.
111. Saigal, S., Feeny, D., Furlong, W., et al. Comparison of the health-related quality of life of extremely low birth weight children and a reference group of children at age eight years. *Journal of Pediatrics* (1994) 125:418-25.
112. *Cardiac surgery in New York State*. Albany: New York State Department of Health, December 1993.

Access to Neonatal Intensive Care

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Abstract

The birth of a high-risk infant is still a relatively rare, not totally predictable event; and the management of high-risk newborns requires highly skilled personnel and sophisticated technology. In the early days of neonatal intensive care, scarce resources led to regionalized systems of neonatal and, later, perinatal services, generally based on voluntary agreements but sometimes reinforced by planning legislation. At present, a vastly increased pool of skilled professionals and technical resources is available in the context of a rapidly changing medical care system characterized by intense competition, coalescence of services under large managed care plans, and substantial cost pressures. The evidence suggests that, in many areas, these forces have led to the dismantling of regional networks; however, the full potential for these changes to hinder or facilitate access to neonatal intensive care remains to be assessed.

The issue of access to special neonatal hospital care emerged only in the twentieth century. Prior to the turn of the century, most births occurred in the home setting, and the limited care repertoire for ill newborns could likewise be provided in that setting. Indeed, it was only in the late 1800s that care of infants less than two years of age was wrested from obstetricians and placed in the domain of pediatricians.¹

In an era when at least 10% of all infants died before their first birthday, the fate of an infant born smaller than average was considered particularly grim and beyond the scope of most medical care. Attempts to improve the outcomes of small babies by providing nutrition and warmth were slow in evolving. Not all such efforts were restricted to medical settings, and popularization of the special care for small newborns was accomplished through exhibits at world's fairs and other such currently unlikely settings.²

In the first half of this century, the place of delivery shifted from home to hospital with the growing realization that

hospital deliveries could reduce the toll of the complications of birth for women. However, birth in a hospital still offered little survival advantage to the low birth weight infant because not much could be done to manage the respiratory distress or hyaline membrane disease that reflected pulmonary immaturity. Despite this lack of success, transport services were organized in some cities, notably Chicago, to bring sick neonates born at home into the hospital for care.²

After World War II, many of the environmental causes of infant mortality past the first month of life had been controlled or reduced by sanitation, immunizations,

and antibiotics. Deaths in the neonatal period began to dominate the rates of infant mortality with low birth weight infants accounting for the majority of these neonatal deaths.³ Thus, the problems of the low birth weight newborn received renewed attention. Until the late 1960s, however, the track record of infant special care units in improving infant outcomes was undistinguished.

Uncritical implementation of interventions poorly grounded in science led to practices that are now seen as useless and silly at best and, in some instances, extremely harmful.⁴ Not only were individual interventions of limited utility, the whole enterprise of special infant care was questionable as neonatal mortality rates remained unchanged for more than 15 years.³

In the late 1960s, however, basic scientific inquiry into the problems of the newborn began to bear fruit in empirically grounded and efficacious interventions. In particular, critical observations about hyaline membrane disease, the major cause of death among premature infants, led to more effective strategies for managing respiratory problems.⁵

While the capability to provide effective, exogenous surfactant, the missing chemical, would come much later (see the article by Horbar and Lucey in this journal issue), basic scientific discoveries led to more efficacious mechanical ventilation techniques.⁶ To underscore the recentness of this success, it should be realized that President Kennedy's son died of hyaline membrane disease in 1963, and the first report of this technique was not published until 1971.⁶

With the advent of more effective management of neonatal problems in the 1970s, the issue of assuring prompt access to infant care units emerged. At this time, access was severely limited by the small number of centers offering specialized newborn services, the few trained specialists, and the related complexity of care. The solution appeared to be nationwide

organization of referrals to the small number of available centers.

Regionalization

The concept of the regionalization of health services is not new. The first articulation of this concept in English was presented to the British Parliament in 1920 in the Report of the Consultative Council on Medical and Allied Services, generally referred to as the Dawson Report. Regionalization was considered to include an organized and integrated hierarchical array of medical services, both preventive and curative. At the base was primary care, consisting of those services most frequently used for common and/or simple health problems. Uncommon or more complex problems were referred to secondary or consultative care, and ultimately to tertiary, usually university-based services.⁷ Explicit in this model was a balance between ready access to care and the efficient deployment of resources at a population level.⁷ During the World War II era in the United States, several states and other jurisdictions experimented with regional plans.⁷ The first attempt to incorporate regional planning nationally occurred in the Hill-Burton Act (Public Law 79-725) in 1946 for hospital construction, and the Heart Disease, Cancer and Stroke Amendments of 1965 (Public Law 89-239) which authorized grants to establish Regional Medical Programs (RMPs) to facilitate access to diagnostic and therapeutic advances in the specified conditions. The voluntary nature of the arrangements, the lack of a clear mission, and the categorical nature of the planning effort limited their success.⁸⁻¹⁰

Subsequent planning legislation—the Comprehensive Health Planning and Public Health Service Amendments of 1966 and the National Health Planning and Resources Development Act of 1974—did not emphasize regionalization as the model of organization.^{8,10} However, they did encourage assessment of health services needs at the state and regional levels

and the development of plans for increasing access to care. Further, some of the regulatory authority for approving major capital expenditures could be used to curtail unneeded expansion of expensive forms of health care such as duplicative intensive care facilities. In some areas, health professionals forged effective alli-

In some areas, health professionals forged effective alliances with planning efforts to foster regionalized neonatal care plans.

ances with planning efforts to foster regionalized neonatal care plans.¹¹ However, the general flaws built into planning legislation precluded universal effectiveness.¹² In the wake of the failure of national planning efforts, alternative approaches emerged to the organization of health services generally.¹³

Regionalization and NICU Care

In the absence of strong national planning for all health services, increasing access to neonatal care relied on voluntary efforts led by health professionals, who noted the experience of a few major centers, and on a more general perception that neonatal care was becoming beneficial. In 1973, Schlesinger cited the improved survival documented in certain centers and recom-

mended the models in Wisconsin, the Province of Quebec, and Arizona for moving sick neonates to special care.¹⁴ The specific rationale for such organizations was the dearth of physicians and nurses skilled in the new techniques and other support services as delineated carefully by Dwyer¹⁵ and endorsed by the American Medical Association House of Delegates.¹¹

The major elements of such regional programs included the structure and function of neonatal intensive care units (NICUs), the formalization of arrangements with referring obstetric units, and transportation systems for sick neonates.^{11,14,15} In this early view, regionalization essentially involved interhospital transfer of infants from community hospitals to the medical center and some reverse outreach educational services to the community hospitals on stabilization of the acutely ill newborn. In some instances, health professionals were able to use federal planning legislation to activate these regionalization efforts;¹¹ in other instances, more informal arrangements among groups of hospitals occurred.

The regionalization of neonatal care represented only a small segment of regionalized services as envisioned by the Dawson model and, moreover, provided little threat to existing care arrangements. The mother remained in the care of her obstetrician. The newborn usually had no primary pediatrician. The limited number of highly trained NICU physicians and

nurses precluded rapid increase in NICUs at the community level. Even among insured couples, coverage for expensive care for sick newborns might not be adequate, and thus, the transfer of such care provided little financial threat to the referring hospitals.

Evidence of the effectiveness of such regional models of neonatal intensive care is sparse. Arguments for its importance rest largely on decreases in neonatal mortality rates after the introduction of NICU care in geographically defined regions where it was not previously available^{14,16,17} and improvements in survival for infants with hyaline membrane disease among those managed through a formal referral system as compared with those managed through other arrangements.¹⁸

Regionalization and Perinatal Care

Evidence also accumulated that outcomes could be improved further by earlier identification of high-risk pregnancies and referral to tertiary perinatal centers before delivery. For example, very low birth weight infants born in hospitals with NICUs did better than those not born in such centers,^{19–21} even accounting for the availability of neonatal transfer.²² Additional evidence was seen in the more favorable outcomes of infants whose mothers were transported to perinatal centers before delivery compared with infants transported after birth.^{23–25}

In response, the notion of regionalized care was expanded to include the prenatal period. Such regional systems would address the needs of all pregnant women in a population through systematic risk assessment and referral to the appropriate consultants when problems emerged. These systems would also assure community providers ready access to consultation, special laboratory facilities, and ongoing education. The intent was to improve perinatal care at all levels for a defined region based on the experience of several programs.^{26–28} The evolving concept of perinatal regionalization thereby broadened to include a large array of services (see Table 1) with a fully integrated system of consultation, referral, and transport, as advocated in several commentaries and editorials,^{11,27,29} and codified by a committee of the major pediatric, obstetric, and nursing organizations in a March of Dimes-sponsored publication entitled *Toward Improving the Outcome of Pregnancy*.³⁰ This manifesto specified in detail the services

Table 1

Characteristics of Regionalized Perinatal Systems	
Characteristic	Related Endnote Numbers*
Neonatal care	
Infant transport	26, 82, 83
Telephone hot lines	84
Outreach education	85, 86
Regionalized follow-up	87, 88
Convalescent back-transfer	45, 46, 47
Maternal care	
Consolidation of maternity services	28
Uniform risk screening	89, 90
Antepartum consultation and referral	92
Maternal transport	23, 24, 25, 92
Regional administration	
Designation of levels of care	11, 15, 30, 52
Standardization of medical records	93
Regional bed planning	14, 28, 30, 54, 55
Regional statistical reporting	37, 38
Regional quality assurance	29, 76, 77
*See the related endnote numbers at the end of this article for complete citations.	

required for level 1, 2, or 3 perinatal care as well as guidelines for delivery volume and/or geographic necessity for each level of care.

In contrast to the relatively sparse data on neonatal systems, more substantial evidence on the effectiveness of these comprehensive perinatal systems is available. To assess the effect of regionalization on previously less-well-organized areas, the Robert Wood Johnson Foundation conducted an eight-site, five-year demonstration program. The evaluation of that program revealed that regionalization occurred and that the rapidity of regionalization was closely correlated with the rate of decline in neonatal mortality, as measured by the proportion of low and very low birth weight infants born in tertiary centers. The sharp decreases in neonatal mortality were not offset by increases in infant

morbidity. Unfortunately, the national movement toward regionalization had become so widespread that a specific effect of the demonstration program could not be detected when compared with the progress in similar control regions not funded by the foundation.³¹ Another Robert Wood Johnson Foundation program, aimed at improving care in 10 rural sites by fostering improved linkages with tertiary centers, also resulted in improved neo-

strategies began to place stresses on regional programs. The current status is summarized in the following section.

Although state planning agencies and health departments could provide reinforcement to regionalization through funding and certification of need authorization, regional perinatal care could best be described as voluntary associations among hospitals and providers. In the 1970s these voluntary associations were reinforced by the impetus toward centralized planning noted above, the scarcity of skilled perinatal and neonatal personnel, the complexity and expense of well-equipped units, more reliable funding through public and private payers, and perhaps also the malpractice crisis. Beginning in the early 1980s, even as the evidence of effectiveness began to accumulate, other forces placed stress on regional programs.

Expansion of Perinatal and Neonatal Intensive Care

During the 1970s and 1980s, both the number of specialized physicians, or neonatologists, and the number of NICUs and NICU beds increased dramatically. This change in availability of NICU care has received little empirical examination, in part because of the difficulty of tracking the information. This dearth of information is soon to be remedied with a directory of neonatologists prepared under the sponsorship of the Section on Perinatal Pediatrics of the American Academy of Pediatrics and expected to be available in the spring of 1995.⁵⁰

While data are still being accumulated, preliminary information reveals that, overall, about 3,000 neonatologists are active in the United States, or about 7.4 per 10,000 live births. In 1994, about 500 hospitals reported having a NICU for a total of about 12,000 NICU beds, or 3 per 1,000 live births.⁵⁰ The number of neonatologists per 10,000 live births is at least twice that of several other industrialized countries⁵¹ and exceeds the upper bound estimate calculated by the American Academy of Pediatrics in 1985 of 5 per 10,000 live births.⁵² However, the rate of very low weight births has been increasing, and the birth weight at which survival is now more routine is decreasing. These trends indicate that the need for neonatologists may exceed 1985 estimates. To what extent the current status represents an excess needs to be examined further.

Regionalization occurred, reinforced by the general impetus to central planning and scarcity of resources.

natal outcomes.³² In addition, reports accumulated on the success of individual programs and on specific aspects of regionalized programs.³³⁻³⁹

While clearly improving infant outcomes, the regional coordination of services and transfer of patients was not without adverse effects. These included:

- initial separation of the newborn from its family and the resulting anxiety and, in some instances, grief experienced by one or both parents,^{40,41}
- prolonged neonatal hospital stays and the financial and emotional costs associated with frequent visiting,⁴²
- disruption of established patient-physician relationships,⁴³
- loss of local medical services,⁴⁴
- disruption of continuity of care and parent-provider relationships through retro-transport to community hospitals to alleviate NICU crowding⁴⁵ even though this is a cost-effective strategy for convalescent care.^{46,47}

Despite these disadvantages, regionalization occurred, reinforced by the general impetus to central planning and scarcity of resources. Other reinforcements included more reliable funding through both public and private payers⁴⁸ and, perhaps, the malpractice crises which made practitioners more cautious in the management of high-risk obstetric patients.⁴⁹

The Current Era

In the early 1980s, changes in the availability of resources and cost containment

The availability of NICU beds is also difficult to assess. The reported number of about 3 per 1,000 live births exceeds the estimated need of one NICU bed per 1,000 live births. However, it is within the overall estimates of 5 to 6 total beds per 1,000 live births, which includes intermediate or convalescent beds.⁵³⁻⁵⁵ While these preliminary data are subject to some error and the shift in care patterns may indicate some increased need for resources over prior estimates, NICU care is no longer a scarce resource nationally, although access to care may not be uniform for all groups because of geographic factors and some of the financing issues discussed below.

Financing Neonatal Care

The growth of NICUs has occurred during an era when the financing of obstetric and newborn services was itself in rapid flux. Financing has become a dominant factor in determining both availability and access because of the exceedingly high cost of neonatal intensive care and the impact of inadequate reimbursement on regional neonatal services.

Private Insurance

Early studies of NICU care⁵⁶ indicated incomplete private insurance coverage with a large pool of uncompensated care. More recent data reveal that, even for privately insured patients, most plans do not begin to cover the full costs of maternity care, and many women are uninsured. For those eligible, services may be covered by Medicaid, but reimbursement is often at considerably lower rates than are typical of private insurance.⁴⁸ Thus, a substantial portion of NICU care remains uncompensated, and the costs of this care are shifted to other payers.^{48,57} Strong evidence indicates that uninsured newborns receive less care than those privately insured or on Medicaid, even when the numbers are adjusted for illness severity.⁵⁸

Absent national health care reform, the current changes in private insurance coverage suggest that the problems of financing neonatal intensive care are likely to grow worse. Employed young couples are most likely to lack employer-based insurance because they have entry level jobs or work in small businesses. Even if the employed parent is covered, dependency coverage is decreasing. The result is that private insurance coverage for children has declined substantially.⁵⁹ What coverage does exist may be exhausted by the

catastrophic costs of NICU admission, as such care has been demonstrated to account for a substantial number of all episodes of catastrophic illness.^{60,61}

Public Financing

Some portion of this financial burden may be offset by recent major expansions of public financing of perinatal care. First, the high cost of neonatal intensive care can result in rapid spend-down to medically needy status for Medicaid coverage, even for the insured population. Second, many states have expanded medical assistance coverage of pregnant women as a means of ensuring adequate prenatal care, and this coverage is automatically extended to their newborns.⁶² Likewise, recent changes in criteria for supplemental Social Security may provide support—both income and access to Medicaid—for children deemed disabled.⁶³

Publicly financed health care is a fragile and vulnerable source of support, however. Eligibility requirements are based on income and vary by state. With the recent downturn in the economy, many states face severe economic constraints in providing for Medicaid patients. While the majority of Medicaid dollars go to support nursing home care for the elderly, few politicians are willing to face such a powerful lobby. Thus, attempts to reduce Medicaid costs focus on the smaller frac-

The current changes in private insurance coverage suggest that the problems of financing neonatal intensive care are likely to grow worse.

tion going to poor women and children. Because neonatal intensive care represents a significant portion of hospital care for children, it has become a target for reducing Medicaid costs, as indicated by the recent Oregon waiver proposal that set birth weight limits for initiating intensive care.

Prospective Payment Systems

The shift to case-based reimbursement under Medicare does not directly affect newborns. However, the adoption of diagnosis-related groups (DRGs) by Medical Assistance (Medicaid) in several states has produced serious problems because the original neonatal DRGs were seriously

Table 2

Effects of Managed Care on Regionalization	
Advantages	Disadvantages
Centralizaion/consolidation of obstetrics and pediatrics	Potential overbuilding of perinatal facilities
Coordination of pediatric care	Redirection of referral patterns
Concentration of research and education	Inconvenience/restricted access
Cost efficiencies	Cost shifting
Standardization of practice	Avoid regional leadership costs (outreach/transport)
Promotion of convalescent transfers	Avoid regional training costs (MDs, NNPs)
Reduced length of stay	Exclusion from infant follow-up
Efficient use of subspecialty services	Inhibition of convalescent transfers
	Restrictions on data availability

flawed.⁶⁴⁻⁶⁷ Specifically, the original DRGs reflected only the experience of community-based hospitals and the limited data available in the small sample of hospitals used to derive the DRGs.

There are several problems related to the use of DRGs as the basis for reimbursement of NICU care. First, these DRGs performed poorly in explaining resource use because they lacked birth weight, a key predictor of cost. Second, for highly regionalized care such as NICUs, all outliers were concentrated in a few centers. A third serious flaw was the disincentive for back-transfer. While DRGs were adopted in only a few states, the threat of their use by other states and by private insurers sparked great

impact of case-based reimbursement in its more refined form remains to be determined. Other pressures on the arrangements of perinatal services come from the massive changes in organization that are being seen generally in health care. In particular, these changes involve rapid emergence of managed care and intense competition among providers to secure plan contracts.

Organization of Services

Managed Care

Managed care plans have expanded from the more traditional health maintenance organization (HMO) to include a broader array of service and financial arrangements. Significant elements of managed care plans include arrangements with selected care providers, utilization review, and strong financial incentives for members to use selected providers and to follow designated procedures.⁶⁹ The major strategy to reduce costs is a reduction in hospital admissions, as well as more prudent purchasing of lower cost or discounted services. The extent to which such plans do reduce costs, the implications of more active management of clinical care, and the relative advantages of various models remain open to question.⁷⁰

Neonatal intensive care admissions are virtually all emergent so it may be difficult to reduce them. Where managed care may influence access to NICU services is its ability to channel obstetric and newborn patients to specific facilities and providers and, thereby, to have a major effect on

The extent to which managed care plans do reduce costs, and the implications of more active management of clinical care remain open to question.

concern among regional centers. This concern prompted the National Association of Children's Hospitals and Related Institutions (NACHRI) to develop pediatric modified DRGs in which the original seven DRGs were expanded to 46 categories, determined by birth weight and need for surgery and/or mechanical ventilation.⁶⁸ Although the modified DRGs are an enormous improvement, they have not been broadly adopted by payers. Thus, the

Table 3

Effects of Competition on Regionalization	
Advantages	Disadvantages
Responsiveness to community providers Improved outreach More responsive transport teams Shorter travel time for patients Hospital support for NICU mission Staffing Equipment	Redundant facilities—increased costs Smaller NICUs—inefficiencies of size Limited subspecialty backup (surgical, genetics, etc.) Dispersion of high-risk patients Limits trials of new technologies Reduces training opportunities Fragments neonatal follow-up Hinders statistical reporting Impairs quality assurance efforts Financial stress on perinatal center “Cream skimming” by peripheral hospitals Rising overhead to maintain transport/outreach

reinforcing or weakening regionalized care (see Table 2).

A major concern is that managed care organizations will direct all obstetric care into lower level hospitals because of their significantly lower operating cost, despite the strong evidence of better outcomes in higher level facilities. The increasing market penetration by managed care in many regions indicates that this will be an important factor in coming decades.

Competition

In view of the changes described above, both insurance plans and providers are now competing heavily for patients. Competition is particularly keen for obstetric patients because hospitals recognize that women make most of the medical care decisions and that a positive birth experience may ensure family loyalty to a particular institution. While competition may drive individual hospitals to upgrade their services, it has also spurred the rapid proliferation of NICUs, particularly for suburban areas where competition for well-insured patients is strongest. These NICUs are established to provide a sense of security in the availability of intensive care if needed but are often small and, therefore, inherently inefficient, although they may operate profitably by attracting a profitable case mix of insured patients. The loss of these patients has further

eroded the financial viability of regional centers⁵⁷ and has begun to redefine them as level 4, or “quaternary,” centers, receiving a declining number of only the smallest infants or those with complex multispecialty needs. This reduced and very expensive population base cannot support the overhead costs of sustaining regional organization including outreach education, consultation, transport, and infant follow-up. The competition among hospitals has also curtailed the cooperative arrangements underlying regional perinatal organizations. Furthermore, the dispersion of patients into many small NICUs will significantly hinder research, medical education, and outcomes evaluation (see Table 3). While competition has also tended to sustain inefficient small obstetric services in suburban markets to draw the loyalty of women clients, in both inner cities and rural areas, competition may lead to closure of community obstetric services, thereby reducing access to prenatal care.

Deregionalization

The aggregate effect of these changes in manpower, facilities, technology diffusion, financing, competition, and health care organization has been a cessation or even reversal of the general trend toward regionalization. This deregionalization

has been noted in several studies. The National Perinatal Information Center studied six regions using in-depth interviews with hospital executives, neonatologists, and obstetricians. While there was great variation from region to region, most agreed there was a general deterioration in perinatal regionalization, that competition had replaced cooperation, and that traditional levels of care were blurring as all facilities escalated the level of care provided. These trends also occurred in many community hospitals where the volume of patients was inadequate to maintain professional skills or provide a cost-effective revenue base.⁷¹ Another study of the Hartford region identified similar concerns, centered on the balance between competition and cooperation. It noted the potential for dispersing the NICU population into smaller competing NICUs versus a single unresponsive monopoly on regionalized services.⁷² Similar concerns have been voiced by others who have called for negotiated cooperation agreements in place of traditional regionalization schemes.⁷³ Interestingly, deregionalization following National Health Service reforms in the United Kingdom has also

dundant services may actually strengthen the regionalization of perinatal care. This level of integration, however, may not be achieved in many regions, and even where it is, the transition may cause serious dislocations for perinatal care.

Conclusion and Recommendations

The rapid proliferation of trained professionals and the diffusion of technology in a context of major organizational change and new financial pressures would appear to signal the unraveling of early regionalized models of delivering care. Little empirical evidence exists, however, to estimate the effect of these changes. Moreover, changes in access to NICU care in response to the various pressures noted above are unlikely to be uniform and will depend on demographics, geography, malpractice experience, and state regulatory environments. Several courses of action are recommended to assure access to appropriate levels of neonatal care.

Access and Equity

The first of these recommendations is for ongoing surveillance of access to NICU care through vital statistics and other record systems. Abundant evidence indicates that higher levels of care are associated with better outcomes.^{21,31,32,75} Shifts in births to lower level hospitals for cost reasons may have a significant impact on overall outcomes. Competition will close not only inefficient services but also poorly reimbursed ones. Hospitals caring for poor and underinsured populations will be stressed regardless of quality or efficiency. To the extent efficiency is also achieved through consolidation of existing facilities, the burden of seeking alternative services may be carried disproportionately by disadvantaged and/or rural communities. Thus, relevant public health and professional organizations should be routinely assessing births and birth-weight-adjusted mortality by hospital of delivery for the newborn population as a whole and for high-risk subgroups.

Quality of Care

The second recommendation is for rapid expansion in rigorous examination of the quality of NICU care. Even among designated tertiary hospitals, there have been instances where quality of NICU care has been questioned,^{76,77} and such quality differences in the past have been more likely

Regionalized perinatal care is also inherently cost effective, utilizing graded levels of care according to need.

produced adverse effects on perinatal care.⁷⁴ These issues provoked the Committee on Perinatal Health to reconvene to formulate an agenda for regionalization in the 1990s and beyond.⁷⁵ They recommended improvements in health education, prenatal care, system organization, access to inpatient and specialty services, documentation and evaluation, and adequate financing of perinatal care.

The reality of perinatal regionalization is that market forces are forcing hospital closures, consolidations, and mergers. Patients are increasingly channeled by payer-provider negotiations rather than historical regional designations. However, the long-term outcome may not be bad. Consolidated obstetric services are inherently safer and more efficient. Regionalized perinatal care is also inherently cost effective, utilizing graded levels of care according to need. The development of highly integrated vertical networks that eliminate re-

to occur in areas serving largely minority populations.⁷⁷ However, variations also occur in units where the level of practice is assumed to be high,^{78,79} suggesting that some portion of the variation may reflect practice patterns, as well as differences in the population that is served. The proliferation of small NICUs has raised additional questions about the extent to which such small units will have sufficient numbers of patients to maintain the skills of providers.⁷⁷⁻⁸⁰

To preserve quality in this rapidly changing health care environment, it is necessary first to measure it. This seemingly simple task has not yet been achieved for perinatal care. It is vital to develop comprehensive case mix adjustment tools^{77,81} and to pursue comparative outcomes research.^{78,79} Incorporated into these quality assessments must be explicit recognition of costs. The third-party payers will demand quality at the lowest price.

Adequate Reimbursement

Perinatal and neonatal services remain underfinanced even among populations with insurance. In the current competitive atmosphere, hospitals will be unable to subsidize these services. Besides the support of direct medical services, however, adequate support of other services formerly provided in regionalized networks is necessary (see Table 1). Particularly vulnerable are consultation services, outreach education, assessment of outcomes among discharged children, development and maintenance of information systems, and surveillance and planning activities. Adequate reimbursement must also reflect the increased costs of caring for many high-

risk newborns, especially among the disadvantaged population.

Training

Finally, some equilibrium between the needs of training programs and the need for skilled neonatal professionals must be achieved. This equilibrium will require alterations in the size, number, and staffing

The current changes in neonatal care provide both exciting new opportunities to maximize its utility and grave challenges in assuring equity.

of teaching hospitals. In addition, it may also require the provision of new training experiences to assure the ongoing assessment of neonatal practices as noted above.

In the absence of significant reductions in prematurity rates, NICU care will continue to be needed. Moreover, even with reduced rates of prematurity, such units are also critical to the well-being of children with malformations and acute complications of the newborn period. The current changes in neonatal care provide both exciting new opportunities to maximize its utility and grave challenges in assuring equity.

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1. Smith, C.A. *The Children's Hospital of Boston: "Built better than they knew."* Boston: Little, Brown, 1983.
2. Cone, T.E. *The history of the care and feeding of the premature infant.* Boston: Little, Brown, 1985.
3. Shapiro, S., Schlesinger, E.C., and Nesbitt, R.E.L. *Infant, perinatal, maternal and childhood mortality in the United States.* Cambridge, MA: Harvard University Press, 1968.
4. Silverman, W.A. *Retrolental fibroplasia: A modern parable.* New York: Greene and Stratton, 1980.
5. Avery, M.E., and Mead, J. Surface properties in relation to atelectasis and hyaline membrane disease. *American Journal of Diseases of Children* (1959) 97:517-23.
6. Gregory, G.A., Kitterman, J.A., Phibbs, R.H., et al. Treatment of idiopathic respiratory-distress syndrome in continuous positive airway pressure. *New England Journal of Medicine* (1971) 284:1333-40.
7. Pearson, D.A. The concept of regionalized personal health services in the United States, 1920-1955. In *The regionalization of personal health services.* E.W. Saward, ed. New York: Prodist, 1976, pp. 3-51.

8. Yordy, K.D. Regionalization of health services: Current legislative directions in the United States. In *The regionalization of personal health services*. E.W. Saward, ed. New York: Prodist, 1976, pp. 201–15.
9. Komaroff, A.L. Regional medical programs in search of a mission. *New England Journal of Medicine* (1971) 284:758–64.
10. Batistella, R.M. The course of regional health planning: Review and assessment of recent federal legislation. *Medical Care* (1967) 5:149–61.
11. Butterfield, L.J. Organization of regional perinatal programs. *Seminars in Perinatology* (1977) 1:217–33.
12. Vladick, B.C. Interest-group representation and the HSAs: Health planning and political theory. *American Journal of Public Health* (1977) 67:23–29.
13. Roemer, R., Kramer, C., and Frink, J.E. *Planning urban health services: From jungle to system*. New York: Springer, 1945.
14. Schlesinger, E.R. Neonatal intensive care: Planning for services and outcomes following care. *Journal of Pediatrics* (1973) 82:916–20.
15. Dwyer, P.R. The regional organization of special care for the neonate. *Pediatric Clinics of North America* (1970) 17:761–76.
16. Usher, R.H. Clinical implications of perinatal mortality statistics. *Clinical Obstetrics and Gynecology* (1971) 14:885–25.
17. Horwood, S.P., Boyle, M.H., Torrance, G.W., and Sinclair, J.C. Mortality and morbidity of 500- to 1499-gram birth weight infants live-born to residents of a defined geographic region before and after neonatal intensive care. *Pediatrics* (1982) 69:5:613–20.
18. Vogt, J.F., Chan, L.S., Wu, P.Y.K., and Howes, W.E. Impact of a regional infant dispatch center on neonatal mortality. *American Journal of Public Health* (1981) 71:577–82.
19. Williams, R.L., and Howes, W.E. Cesarean section, fetal monitoring, and perinatal mortality in California. *American Journal of Public Health* (1979) 68:864–70.
20. Hein, H.A., and Brown, C.J. Neonatal mortality review: A basis for improving care. *Pediatrics* (1981) 68:504–9.
21. Paneth, N., Kiely, J.L., Wallenstein, S., et al. Newborn intensive care and neonatal mortality in low-birth-weight infants: A population study. *New England Journal of Medicine* (1982) 307:149–55.
22. Paneth, N., Kiely, J.L., and Susser, M. Age at death used to assess the effect of interhospital transfer of newborns. *Pediatrics* (1984) 73:854–61.
23. Harris, T.R., Isaman, J., and Giles, H.R. Improved neonatal survival through maternal transport. *Obstetrics and Gynecology* (1978) 52:294–300.
24. Modanlou, H.D., Dorchester, W., Freeman, R.K., and Rommal, C. Perinatal transport to a regional perinatal center in a metropolitan area: Maternal versus neonatal transport. *American Journal of Obstetrics and Gynecology* (1980) 138:1157–64.
25. Levy, D.L., Noelke, K., and Goldsmith, J.P. Maternal and infant transport program in Louisiana. *Obstetrics and Gynecology* (1981) 57:500–504.
26. Gluck, L. Design of a perinatal center. *Pediatric Clinics of North America* (1970) 17:777–91.
27. Merkat, I.R., and Johnson, K.G. Regionalization of perinatal care for the United States. *Clinics in Perinatology* (1976) 3:271–76.
28. Ryan, G.M. Regional planning for maternal and perinatal health services. *Seminars in Perinatology* (1977) 1:255–66.
29. Lucey, J.F. Why we should regionalize perinatal care. *Pediatrics* (1973) 52:488–91.
30. National Committee on Perinatal Health. *Toward improving the outcome of pregnancy*. White Plains, NY: National Foundation–March of Dimes, 1976.
31. McCormick, M.C., Shapiro, S., and Starfield, B.H. The regionalization of perinatal services: Summary of the evaluation of a national demonstration program. *Journal of the American Medical Association* (1985) 253:799–804.
32. Gortmaker, S.L., Clark, C.J.G., Graven, S.N., et al. Reducing infant mortality in rural America: Evaluation of the Rural Infant Care Program. *Health Services Research* (1987) 22:91–116.
33. Hein, H.A., and Lathrop, S.S. The changing pattern of neonatal mortality in a regionalized system of perinatal care. *American Journal of Diseases of Children* (1986) 140:989–93.

34. Meuli, R.L., and Cohen, L.J. Regionalization of perinatal care. *Western Journal of Medicine* (1984) 141:695–98.
35. Rosenblatt, R.M., Mayfield, J.A., Hart, G., and Baldwin, L.M. Outcomes of regionalized perinatal care in Washington state. *Western Journal of Medicine* (1988) 149:98–102.
36. Siegel, E., Gettings, D., Campbell, S., and Gerild, P. A controlled evaluation of rural perinatal care: Impact on mortality and morbidity. *American Journal of Public Health* (1985) 75:246–53.
37. Powers, W.F., Hegwood, P.D., and Young, S.K. Perinatal regionalization as measured by antenatal referral. *Obstetrics and Gynecology* (1988) 71:375–79.
38. Gagnon, D.E., Allison-Cooke, S., and Schwartz, R.M. *Evaluation of the states and effectiveness of perinatal regionalization: Final report*. (SCC: #90539, RFP: #601-712-90-1). Providence, RI: National Perinatal Information Center, 1991.
39. South Carolina Regionalization Surveillance System. *Report of the perinatal indicators for 1983–1991*. Vols. 1 and 2. Columbia: South Carolina Department of Health and Environmental Control, December 1992.
40. Benfield, D.G., Leib, S.A., and Ruster, J. Grief response of parents after referral of the critically ill newborn to a regional center. *New England Journal of Medicine* (1976) 294:975–78.
41. Klaus, M.H., and Kennell, J.H. Mothers separated from their newborn infants. *Pediatric Clinics of North America* (1970) 17:1015–37.
42. McLoughlin, A., Hillier, J.F., and Robinson, M.J. Parental costs of neonatal visiting. *Archives of Disease in Childhood* (1993) 68:597–99.
43. Klein, M.C., and Papageorgiu, A.N. Can perinatal regionalization be reconciled with family-centered care? *Journal of Family Practice* (1977) 5:969–74.
44. Donahue, C.L., Pettigrew, A.I.T., Young, K., and Ryan, G.M. The closure of maternity services in Massachusetts: The causes, process and hospital impact. *Obstetrics and Gynecology* (1977) 50:280–84.
45. Jung, A.L., and Bose, C.L. Back transport of neonates: Improved efficiency of tertiary nursery utilization. *Pediatrics* (1983) 71:918.
46. Bose, C.L., LaPine, T.R., and Jung, A.L. Neonatal back-transport: Cost-effectiveness. *Medical Care* (1985) 23:14–19.
47. Phibbs, C.S., and Mortensen, L. Back transporting infants from neonatal intensive care units to community hospitals for recovery care: Effect on total hospital charges. *Pediatrics* (1992) 90:22–26.
48. Gold, R.B., Kenney, A.M., and Singh, S. *Blessed events and the bottom line: Financing maternity care in the United States*. New York: Alan Guttmacher Institute, 1987.
49. Rastow, V.P., Osterweis, M., and Bulger, R.J. Medical professional liability and the delivery of obstetrical care. *New England Journal of Medicine* (1989) 321:1057–60.
50. Personal communication with the organizing committee for the 1995–1996 neonatologists directory and D. Bhatt, December 1994.
51. Silverman, W.A. Is neonatal medicine in the United States out of step? *Pediatrics* (1993) 92:612–13.
52. American Academy of Pediatrics, Committee on Fetus and Newborn. Manpower needs in neonatal pediatrics. *Pediatrics* (1985) 76:132–35.
53. American Academy of Pediatrics, Committee on Fetus and Newborn, Committee of the Section on Perinatal Pediatrics. Estimates of need and recommendations for personnel in neonatal pediatrics. *Pediatrics* (1980) 65:850–53.
54. American Academy of Pediatrics. *Guidelines for perinatal care*. Evanston, IL: AAP, 1983.
55. Jung, A.L., and Streeter, N.S. Total population estimate of newborn special care needs. *Pediatrics* (1985) 75:993–96.
56. McCarthy, J.T., Koops, B.L., Honeyfield, P.R., and Butterfield, L.J. Who pays the bill for neonatal intensive care? *Journal of Pediatrics* (1979) 95:755–61.
57. Immershein, A.W., Turner, C., Wells, J.G., and Pearman, A. Covering the costs of care in neonatal intensive care units. *Pediatrics* (1992) 89:56–61.
58. Braveman, P.A., Egerter, S., Bennett, T., and Showstack, J. Differences in hospital resource allocation among sick newborns according to insurance coverage. *Journal of the American Medical Association* (1991) 266:3300–3308.
59. Cunningham, P.J., and Monheit, A.C. Insuring the children: A decade of change. *Health Affairs* (1990) 9,4:76–90.

60. Schroeder, S.A., Showstack, J.A., and Roberts, H.E. Frequency and clinical description of high-cost patients in 17 acute-care hospitals. *New England Journal of Medicine* (1979) 300:1306–9.
61. Zook, C.J., and Moore, F.D. High-cost users of medical care. *New England Journal of Medicine* (1980) 302:996–1002.
62. Gold, R.B., Singh, S., and Frost, J. The Medicaid eligibility expansions for pregnant women: Evaluating the strength of state implementation efforts. *Family Planning Perspectives* (1993) 25:196–207.
63. Perrin, J.M., and Stein, R.E.K. Reinterpreting disability: Changes in supplemental security income for children. *Pediatrics* (1991) 88:1047–51.
64. Lagoe, R.J., Milliren, J.W., and Baader, M.J. Impact of selected diagnosis-related groups on regional neonatal care. *Pediatrics* (1986) 77:627–32.
65. Resnick, M.B., Ariet, M., Carter, R.L., et al. Prospective pricing system for tertiary neonatal intensive care. *Pediatrics* (1986) 78,5:820–28.
66. Phibbs, C.S., Phibbs, R.H., Pomerance, J.J., and Williams, R.L. Alternative to diagnosis-related groups for newborn intensive care. *Pediatrics* (1986) 78,5:829–36.
67. Poland, R.L., Bollinger, R.O., Bedard, M.P., and Cohn, S.N. Analysis of the effects of applying federal diagnosis-related grouping (DRG) guidelines to a population of high-risk newborn infants. *Pediatrics* (1985) 76:104–9.
68. Lichtig, L.K., Knauf, R.A., and Barteletti, A. Revising diagnosis-related groups for neonates. *Pediatrics* (1989) 84:49–61.
69. Hoy, E.W., Curtis, R.E., and Rice, T. Change and growth in managed care. *Health Affairs* (1991) 10,4:18–36.
70. Miller, R.H., and Luft, H.S. Diversity and transition in health insurance plans. *Health Affairs* (1991) 10,4:37–47.
71. Cooke, S.A., Schwartz, R.M., and Gagnon, D.E. *The perinatal partnership: An approach to organizing care in the 1990s*. Project #12129. Providence, RI: National Perinatal Information Center, 1988.
72. Richardson, D.K., Reed, K., Cutler, J.C., et al. Perinatal regionalization versus hospital competition: The Hartford example. *Pediatrics* (1995) in press.
73. Kanto, Jr., W.P. Regionalization revisited. Editorial. *American Journal of Diseases of Children* (1987) 141:403–4.
74. Pope, C., and Wild, D. Putting the clock back 30 years: Neonatal care since the 1991 NHS reforms. *Archives of Diseases in Childhood* (1992) 67:879–81.
75. National Committee on Perinatal Health. *Toward improving the outcome of pregnancy: The 90s and beyond*. White Plains, NY: March of Dimes Birth Defects Foundation, 1993.
76. Greenland, S., Watson, E., and Neutra, R.R. The case-control method in medical care evaluation. *Medical Care* (1981) :872–88.
77. International Neonatal Network. The CRIB (clinical risk index for babies) score: A tool for assessing initial neonatal risk and comparing performance of neonatal intensive care units. *Lancet* (1993) 342:193–98.
78. Investigators of the Vermont-Oxford Trials Network Database Project. The Vermont-Oxford Trials Network: Very low birth weight outcomes for 1990. *Pediatrics* (1993) 91:540–45.
79. Hack, M., Horbar, J.D., Malloy, M.H., et al. Very low birthweight outcomes of the NICHD Neonatal Network. *Pediatrics* (1991) 87:587–97.
80. Farley, D.E., and Ozminkowski, R.J. Volume-outcome relationships and in-hospital mortality: The effect of changes in volume over time. *Medical Care* (1992) 30:77–94.
81. Richardson, D.K., Gray, J.E., McCormick, M.C., et al. Score for Neonatal Acute Physiology (SNAP): Validation of a new physiology-based severity of illness index. *Pediatrics* (1993) 91:617–23.

Sources for Tables 1–3:

82. Chance, G.W., Matthew, J.D., Gash, J., et al. Neonatal transport: A controlled study of skilled assistance. *Journal of Pediatrics* (1978) 93:662–66.
83. Pettett, G., Merenstein, G.B., Battaglia, F.C., et al. An analysis of air transport results in the sick newborn infant: Part I. The transport team. *Pediatrics* (1975) 55:774–82.
84. Perlstein, P.H., Edwards, N.K., and Sutherland, J.M. Neonatal hotline telephone network. *Pediatrics* (1979) 64:419–24.
85. Kattwinkel, J., Cook, L.J., Nowacek, G.A., et al. Improved perinatal knowledge and care in the community hospital through a program of self-instruction. *Pediatrics* (1979) 64:451–58.

86. Wirtschafter, D.D., Sumners, J., Jackson, J.R., et al. Continuing medical education using clinical algorithms. A controlled-trial assessment of effect on neonatal care. *American Journal of Diseases of Children* (1986) 140:791–97.
87. Saigal, S., Szatmari, P., Rosenbaum, P., et al. Intellectual and functional status at school entry of children who weighed 1000 grams or less at birth: A regional perspective of births in the 1980s. *Journal of Pediatrics* (1990) 116:409–16.
88. McCormick, M.C. Long-term follow-up of infants discharged from neonatal intensive care units. *Journal of the American Medical Association* (1989) 261:1767–72.
89. Hobel, C.J., Yonkelis, L., and Forsythe, A. Prenatal and intrapartum high-risk screening II: Risk factors reassessed. *American Journal of Obstetrics and Gynecology* (1979) 135:1051–56.
90. Hobel, C.J., Hyvarinen, M.A., Okada, D.M., and Oh, W. Prenatal and intrapartum high-risk screening: I. Prediction of the high-risk neonate. *American Journal of Obstetrics and Gynecology* (1973) 117:1–9.
91. Richardson, D.K., Gabbe, S.G., and Wind, Y. Decision analysis of high risk patient referral. *Obstetrics and Gynecology* (1984) 63,4:496–501.
92. Miller, T.C., Densberger, M., and Krogman, J. Maternal transport and the perinatal denominator. *American Journal of Obstetrics and Gynecology* (1983) 147:19–24.
93. Jennet, R.J., Gall, D., Waterkotte, G.W., and Warford, H.S. A computerized perinatal data system for a region. *American Journal of Obstetrics and Gynecology* (1978) 131:157–63.

Long-Term Developmental Outcomes of Low Birth Weight Infants

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Abstract

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Advances in neonatal medicine have resulted in the increased survival of infants at lower and lower birth weight. While these medical success stories highlight the power of medical technology to save many of the tiniest infants at birth, serious questions remain about how these infants will develop and whether they will have normal, productive lives.

Low birth weight children can be born at term or before term and have varying degrees of social and medical risk. Because low birth weight children are not a homogeneous group, they have a broad spectrum of growth, health, and developmental outcomes. While the vast majority of low birth weight children have normal outcomes, as a group they generally have higher rates of subnormal growth, illnesses, and neurodevelopmental problems. These problems increase as the child's birth weight decreases. With the exception of a small minority of low birth weight children with mental retardation and/or cerebral palsy, the developmental sequelae for most low birth weight infants include mild problems in cognition, attention, and neuro-motor functioning. Long-term follow-up studies conducted on children born in the 1960s indicated that the adverse consequences of being born low birth weight were still apparent in adolescence.

Adverse sociodemographic factors negatively affect developmental outcomes across the continuum of low birth weight and appear to have far greater effects on long-term cognitive outcomes than most of the biological risk factors. In addition, the cognitive defects associated with social or environmental risks become more pronounced as the child ages. Enrichment programs for low birth weight children seem to be most effective for the moderately low birth weight child who comes from a lower socioeconomic group.

Continued research and attempts to decrease the rate of low birth weight and associated perinatal medical sequelae are of primary importance. Ongoing documentation of the long-term outcome of low birth weight children needs to be mandated, as does the implementation of environmental enrichment programs to help ameliorate the long-term consequences for infants who are born low birth weight.

Children born low birth weight constitute a heterogeneous group including children born preterm (at fewer than 37 weeks of gestation), as well as those born at term gestation but subnormal in weight because of various abnormal maternal or fetal conditions (see the article by Paneth in this journal issue). An examination of the long-term outcomes of low birth weight children therefore must include consideration of whether the children were born preterm or at term gestation and the conditions associated with the low birth weight.

This article will review the most recent findings with regard to early childhood and school-age developmental outcomes and health of low birth weight children. First, we provide a historical perspective on current outcomes by summarizing the outcomes of low birth weight children born prior to and after the introduction of neonatal intensive care. Next, we review the methodological issues related to evaluating developmental outcomes of low birth weight children, summarize the data on the long-term outcomes, and discuss some of the risk factors associated with developmental outcome of low birth weight children. Then, we summarize evidence regarding the effectiveness of development enrichment programs for low birth weight children. Finally, we conclude with recommendations for policymakers.

Historical Review of the Outcomes of Low Birth Weight Children

Developmental outcomes of low birth weight children were the subject of concern and review long before the introduction of neonatal intensive care methods.¹

Outcome studies of low birth weight children born before the 1960s included mainly infants with birth weights greater than 1.5 kilograms because very few infants born at lower birth weights survived during this era. In the 1960s, as a result of advances in neonatal intensive care, more infants weighing less than 1,500 grams (3 pounds, 5 ounces) at birth survived. These infants, termed *very low birth weight*, have

been the focus of the majority of studies published during the past 20 years.² Further increases in survival in the late 1970s led to studies of infants with birth weights of less than 1,000 grams (2 pounds, 3 ounces, termed *extremely low birth weight*) and less than 750 grams (1 pound, 10 ounces) who survived.³

Very low birth weight infants are, with few exceptions, all born preterm (at fewer than 37 weeks of gestation); however, many of these infants have also experienced varying degrees of intrauterine growth failure. Follow-up studies based on gestational age rather than on birth weight have rarely been performed, despite the fact that the maturity of the infant at birth, as measured by gestational age, is the major predictor of outcome.⁴ This is primarily due to the lack of accuracy in the assessment of gestational age when the mother has not received prenatal care.⁵

Before the Introduction of Neonatal Intensive Care

In general, low birth weight children born before the introduction of neonatal intensive care had more health and developmental problems than children of normal birth weight (see Box 1). Nevertheless, the development of these low birth weight children fell in the broad normal range, with the exception of very low birth weight children, who had a high rate of neurosensory and developmental handicap.

In evaluating the long-term developmental outcome of low birth weight infants born prior to the neonatal intensive care era, consideration needs to be given to the higher rate of neonatal mortality at

Box 1

Low Birth Weight Outcomes Before Neonatal Intensive Care

High Mortality

Assisted ventilation not used

Very few infants born at less than 28 weeks of gestation and/or with birth weights of less than 1,000 grams survived

Iatrogenic Complications Due to Various Therapies

Follow-Up Outcomes

Descriptive, lacked formal psychometric measures

High rate of cerebral palsy and developmental handicap

Lower intelligence when compared to normal birth weight control groups

Higher rates of learning difficulties, neurological soft signs, and hyperactive behavior, even in children with normal intelligence

Pessimism Concerning These Inferior Outcomes

that time. The survivors thus represented a select population of relatively mature, healthy infants. In 1940, Benton reviewed the literature on the outcomes of low birth weight children prior to this time.¹ Although many of the earlier reports were descriptive and lacked formal psychometric measures, he concluded that children born preterm demonstrate developmental retardation and that the lower the birth weight the greater the retardation. He fur-

Care of low birth weight infants prior to 1940 was conservative with very little intervention.

ther concluded that premature children have higher rates of severe mental defect and that even children considered normal have "nervous traits" including poor sleep, fatigability, irritability, shyness, fearfulness, emotional outbursts, disturbances in concentration and attention, and forgetfulness.

Care of low birth weight infants prior to 1940 was conservative with very little intervention. Between 1940 and 1960, various therapies were instituted, some of which had devastating effects on later de-

velopmental outcomes. These included withholding of early feeding, which led to dehydration and hypoglycemia; liberal use of oxygen, which resulted in retinopathy of prematurity and blindness; antibiotic-related deafness, which was caused by streptomycin; and kernicterus (brain damage due to severe jaundice), which was closely related to the use of sulpha drugs. Reviews published between 1940 and 1960 drew additional pessimistic conclusions about the developmental outcome of low birth weight children.⁶

For example, Lubchenco in Denver reported that, at 10 years of age, 44% of very low birth weight children born between 1947 and 1950 had intelligence quotients (IQs) under 70 (were developmentally impaired), and 12% were blind. Only a third of the children were free of handicap and had IQs in the normal range (higher than 89).⁷ Outcomes were especially poor for very low birth weight children who were affected by the iatrogenic effects of the various care practices described above. These children included mainly those born at birth weights between 1,000 and 1,500 grams (2 pounds, 3 ounces and 3 pounds, 5 ounces) because, at that time, very few children born weighing less than 1,000 grams survived.

During this pre-intensive-care era, the outcomes for moderately low birth weight children (those whose weights were between 1,500 and 2,499 grams) were much better than the outcomes for very low birth weight children; however, they were still inferior to the outcomes for normal birth weight children.

The National Collaborative Study of births between 1959 and 1965 reported a mean IQ at four years of age of 94 for white children born weighing between 737 and 2,000 grams (from 1 pound, 10 ounces to 4 pounds, 7 ounces) compared with an IQ of 101 for those with a birth weight between 2,000 and 2,500 grams (between 4 pounds, 7 ounces and 5 pounds, 8 ounces) and 103 for those with a birth weight between 2,500 and 3,000 grams (between 5 pounds, 8 ounces and 6 pounds, 10 ounces). Corresponding IQs for black children of the same age in these three birth weight groups were 86, 89, and 91, respectively.⁸ Rates of minimal brain dysfunction—including learning difficulties, hyperactive behavior, and neurological soft signs—were also significantly higher in the low birth weight population.⁹

After the Introduction of Neonatal Intensive Care

Very low birth weight children constitute only 1% of all births in the United States and less than 15% of low birth weight births; however, most of the studies conducted after the introduction of neonatal intensive care concentrated on this birth weight subgroup. The majority of preterm, moderately low birth weight infants do not require intensive care and, with few exceptions,¹⁰⁻¹² have not been as well studied. The subpopulation of low birth weight children who were born at term but who were undergrown, or were "small for gestational age," however, has been selectively studied.

The improved survival of very low birth weight infants following the introduction of neonatal intensive care methods during the 1960s was accompanied by a marked decrease in the rates of cerebral palsy and neurodevelopmental handicap.^{2,13} Various innovations in obstetric practice and neonatal intensive care, which prevented brain damage, most likely account for the reduced morbidity in this group of infants (see Box 2). Changes in methods of practice included improved delivery room care and resuscitation, assisted ventilation when needed, umbilical artery catheter placement to monitor oxygenation, intravenous fluid therapy, and exchange transfusions to treat jaundice. Further technological and pharmacological improvements introduced during the 1970s and 1980s included fetal monitoring; more liberal use of cesarean delivery; neonatal monitoring of heart rate, respiration, and blood pressure; intravenous nutrition; phototherapy to treat jaundice; and drugs to treat apnea of prematurity and patent ductus arteriosus, a heart condition.

Survival continued to improve during the 1970s and the 1980s; however, with few exceptions, rates of cerebral palsy and neurodevelopmental handicap in early childhood among very low birth weight children remained essentially unchanged.^{2,14-18} As a result of these trends, there has been an increase not only in the absolute number of surviving children with normal development but also in the number of children with handicapping conditions. An increase in the prevalence of cerebral palsy has been especially apparent and is largely attributable to the improved survival of very low birth weight children. Bhushan estimated that, as a result of the improved survival of low birth weight infants in the United States be-

Box 2

Low Birth Weight Outcomes Following the Introduction of Neonatal Intensive Care

Improved Survival Between 1960 and 1990

Decrease in Rates of Cerebral Palsy and Developmental Handicap between 1960 and 1980

Since 1980

No further improvement in neurodevelopmental outcomes despite continued improved survival

Most low birth weight children function within the normal range

When compared with normal birth weight children, low birth weight children have higher rates of

- Mental retardation
- Cerebral palsy
- Blindness, deafness
- Psychomotor problems
- School failure
- Subnormal growth
- Health problems

tween 1960 and 1986, for every additional child with cerebral palsy, eleven normal healthy children survived.¹⁹

Surfactant therapy was introduced in the late 1980s and has resulted in further improvements in survival but without

The improved survival of very low birth weight infants following the introduction of neonatal intensive care methods during the 1960s was accompanied by a marked decrease in the rates of cerebral palsy and neurodevelopmental handicap.

change in the developmental outcomes of the survivors.²⁰ This will most likely result in a further increase in the numbers of both healthy and handicapped very low birth weight children who have survived in the late 1980s and early 1990s.

Studies of Developmental Outcomes for Low Birth Weight Children

Review of Methodology

Numerous reviews of reported outcomes of low birth weight children have criticized the overall poor quality of studies in this

area and have suggested standards to be observed when undertaking developmental follow up studies.^{1,6,16,17,21-23} Major criticisms include inadequate sample size, heterogeneity of populations, short duration of follow-up, lack of control populations, lack of uniformity in assessment of outcome and definitions of handicap, and questions with regard to the representativeness of study samples and gener-

perimental or exploratory, assessment of the quality of outcomes has never been mandated. National funding has not been readily available, and outcome evaluations have rarely been carried out in a systematic fashion using hypothesis-driven research methodologies.

An additional problem inherent in determining the long-term outcomes of very low birth weight infants is that, by the time meaningful assessments of outcomes such as school-age performance are obtained, neonatal treatment has also changed, and these changes may have affected later outcomes.^{8,29} Changes in the definitions of normal growth and cognitive outcomes over time also limit comparison between studies, as exemplified by the recently revised Bayley Scales of Infant Development, which are currently being used extensively in follow-up studies.

Although neonatal intensive care has, to a large extent, been experimental or exploratory, assessment of the quality of outcomes has never been mandated.

alization of results to other samples. Although such criticism is valid, some of these shortcomings have been unavoidable.

The constitution of some samples, for example, has been determined by enrollment in controlled clinical trials.^{10,20,24} Reports have also included descriptions of longitudinal changes in outcome^{14,15,18,19,25} and cross-sectional observational studies.^{4,13,26} The majority of observational studies published since the 1970s have been attempts to monitor the outcomes associated with neonatal intensive care and to examine specific risk factors.

The planning of such studies has been problematic, partly because advances in technology and new therapies have, with few exceptions (for example, surfactant), been introduced haphazardly and without controlled trials. Thus, it is not surprising that follow-up studies have reported a patchwork of outcomes.²²

The progressive introduction of neonatal intensive care technology has saved the lives of many infants. In most instances, the cost of this care is covered by state and private insurance plans. However, the costs of follow-up care and assessment of outcome are not fully covered.

At best, medical insurance pays only for a clinic visit but not to maintain staff to track these families and ensure that their infant will be available for long-term follow-up. Some states have funded clinical neonatal follow-up; however, the outcomes of these efforts have rarely been published.^{27,28} Although neonatal intensive care has, to a large extent, been ex-

Factors to Consider When Evaluating Long-Term Outcome Studies

There are several factors to consider in evaluating long-term outcome studies (see Box 3). These factors are discussed in the paragraphs that follow.

Survival Rate

High mortality rates may indicate poor perinatal treatment which may have a detrimental effect on the long-term outcome of the survivors. Increased mortality among high-risk infants may also be associated with improved outcomes in the surviving low birth weight children, as those with the potential for a poor outcome may have died.

Representativeness of the Study Sample

The majority of studies have been based on hospital samples that may not be representative of all the survivors in a specific region. Furthermore, hospital-based studies that include infants transported from community hospitals are biased by the selective referral of the sickest infants. Regional outcomes have been examined in Canada, Europe, Australia, and England but rarely in the United States.

Sample Characteristics

Outcomes are likely to vary in relation to differences in how the samples are constituted. Sampling parameters to consider include (1) the range of birth weight and gestational age under study; (2) the rate of intrauterine growth failure; (3) whether children with congenital malformations (for example, Down's syndrome, meningomyelocele) or congenital infections (for

Box 3

Factors to Consider When Evaluating Long-Term Outcome Studies

1. Rate of Survival**2. Type of Study**

Longitudinal

Cross-sectional

Controlled trial or intervention: pharmacotherapeutic (e.g., surfactant) or educational enrichment

Examination of specific risk factors (e.g., brain hemorrhage, chronic lung disease, etc.)

3. Study Sample

Hospital-based or regional

4. Sample Characteristics

Birth weight and gestational age range

Rates of intrauterine complications

Intrauterine growth failure

Intrauterine infections

Congenital malformations

Perinatal morbidity (e.g., periventricular hemorrhage, chronic lung disease)

Sociodemographic descriptors (e.g., sex, race, marital status, education)

Parental substance abuse

Postdischarge medical care and morbidity

Postdischarge intervention or enrichment programs

5. Suitability of Comparison (Control) Groups**6. Rate of Loss of Follow-Up****7. Duration of Follow-Up**

Infancy

Early childhood

School age

8. Correction for Preterm Birth**9. Outcomes Measured**

Growth

Health status

Illness (e.g., respiratory, rehospitalization)

Postdischarge death rates

Neurological status

Cerebral palsy

Blindness

Deafness

Neuropsychiatric outcomes

Intelligence

Speech and language

Psychomotor

Memory

Attention

Academic achievement

School performance

Failure

Need for special education

Behavior

Social competence

Functioning

Activities of daily living

Impact/effect on family

Socioeconomic

Cost of hospital stay

Cost of education

Things to Remember

Exclusion of impaired children may falsely improve outcomes.

Neonatal treatment and survival have improved so rapidly that many results are obsolete by the time the children are old enough to study. Developmental norms of growth and development might also have changed.

example, herpes, congenital cytomegalovirus, syphilis) are included; (4) perinatal and neonatal therapies used and rates of complications (for example, cesarean section, Apgar scores, delivery room resuscitation, periventricular hemorrhage, chronic lung disease); (5) sociodemographic descriptors; (6) behavioral characteristics of the parents, including smoking and drug abuse; (7) post-hospital-discharge medical care and complications; and (8) special interventions or enrichment programs.

The Nature of Control and Comparison Groups

If studies are not composed of randomly assigned intervention and control groups, then differences between the groups being compared must be taken into consideration. At a minimum, study groups should be matched for factors such as race, sex, and parental socioeconomic indices (marital status, age, level of education, and occupation).³⁰

Sample Attrition

Children lost to follow-up are more likely to come from lower socioeconomic groups

who generally have poorer outcomes.^{31,32} If the attrition of children with poorer outcomes does not occur evenly from the study groups, then the study outcomes will be heavily biased.

Duration of Follow-Up

Children must be followed to at least 18 to 24 months to assess severe neurodevelopmental problems. Follow-up to early school age is required to measure more subtle disturbances in areas such as fine motor ability, visual-motor skills, behavior, and learning.

Correction for Preterm Birth

There is, in general, a consensus that the child's age should be calculated from the mother's last menstrual period (postmenstrual age) rather than from birth (postnatal age), at least until the child has a postnatal age of three years.³³

Outcomes Measured

Adverse effects of low birth weight vary in accordance with how outcomes are assessed. Medical outcomes include abnormalities on physical and neurological exams, growth attainment, illness, and re-hospitalizations. Neurological outcomes, such as rates of cerebral palsy or blindness, are not affected by sociodemographic factors and, thus, are good markers of biological risk. Neuropsychological measures that are sensitive to subtle degrees of dysfunction

include intelligence, memory, speech and language, psychomotor abilities, academic achievement, behavior, and attention. Social competence, child temperament, and the impact of having a low birth weight or very low birth weight child on the family system are additional outcomes, but ones rarely considered in research studies.³⁴⁻³⁶ The measurement of functional abilities includes ratings by the physician¹⁴ or caretakers^{11,37} of the child's ability to perform age-appropriate activities of daily living.

Classification of Handicap

The terms *impairment* and *handicap* have been applied loosely, and uniform definitions are lacking. Handicaps generally refer to severe neurosensory diagnoses such as cerebral palsy, blindness, and deafness, and/or to subnormal intelligence. Disabilities of this nature are further classified as mild, moderate, and severe.^{14,38} The World Health Organization Classification of Impairments, Disabilities and Handicaps has been applied in one study.³⁹ Uniform definitions of problems in school functioning are also lacking. Although gross indices of school performance, such as grade repetition and placement in special education, have been most often applied, criteria for these interventions vary across teachers and school districts. Similarly, definitions of specific learning problems vary across studies and school districts.

Exclusions

Children with severe neurosensory or behavioral dysfunction are sometimes excluded from study because of their inability to comply with or understand test instructions. Thus, outcomes reflect the children tested rather than the entire birth weight subgroup. Children with neurological impairment or mental deficiency are also excluded from some studies so that more specific learning problems may be identified.

Outcomes for Low Birth Weight Infants

Low birth weight children experience combinations of various neurosensory, developmental, and health problems which compound the clinical and educational outcomes. In the following section, we describe some of the more common outcomes for infants born at low birth weight.

Table 1

Physical and Neurosensory Impairment by Birth Weight									
Author/ Related Endnote Number*	Year of Birth	Cohort Description	Age, Years	Outcomes Measured	Birth Weight Range, grams				
Hack ⁴³	1977– 1979	Hospital	8	Neurosensory abnormality		<1,500 10%			≥2,500 0%
Saigal ⁴⁰	1977– 1981	Regional	8	Neurosensory sequelae ^a	<1,000 23%				≥2,500 0.7%
McCormick ¹¹	1978– 1981	Multicenter very low birth weight and regional	8–10	Neurologic sequelae ^b	<1,000 21%	1,000 to 1,499 17%	1,500 to 2,499 6%		≥2,500 5%
Teplin ³⁸	1980	Hospital	6	Neurologic exam Normal Suspect Abnormal	<1,000 39% 50% 11%				≥2,500 77% 23% 0%
Petersen ⁴²	1980– 1982	Hospital	4	Normal physical exam Normal neurologic exam Normal eye exam		<1,500 71% 65% 69%	1,500 to 2,300 84% 82% 89%		≥2,500 90% 92% 90%
Hack ⁴⁴	1982– 1986	Regional	7	Cerebral palsy Blindness Deafness	<750 9% 6% 2%	750 to 1,499 6% 2% 2%			≥2,500 0% – –
Scottish ⁴¹	1984	Regional	4 to 5	Neuromotor impairment ^c Blindness Squint (strabismus) Deafness ^d	<1,000 22% 5% 20% 3%	1,000 to 1,499 14% 0.3% 12% 1.4%	1,500 to 1,749 11% 1.2% 9% 2%		

^a Cerebral palsy, hydrocephalus, microcephaly, blindness, and deafness
^b Seizures, epilepsy, hydrocephalus, cerebral palsy, and mental retardation
^c <10 percentile on the Henderson Test of Motor Impairment
^d Requiring hearing aid
 * See the related endnote numbers at the end of this article for complete citation.

Neurosensory Outcomes

Cerebral palsy is the most common major neurological abnormality seen in low birth weight children. The rates of cerebral palsy increase with decreasing birth weight. Despite different definitions and categorization of conditions including cerebral palsy, hydrocephalus, microcephaly, blindness, deafness, and seizures, the overall rates of these conditions are remarkably consistent and range from approximately 20% for children with birth weights of less than 1,000 grams (2 pounds, 3 ounces)^{38,40} to 14% to 17% for children with birth weights of 1,000 to 1,500 grams (from 2 pounds, 3 ounces to 3 pounds, 5 ounces)^{11,41} and 6% to 8% for children with birth weights of 1,500 to 2,499 grams (from 3 pounds, 5 ounces to 5 pounds, 8 ounces).^{11,41,42} (See Table 1.) By comparison, rates below 5% are reported for children of normal birth weight.^{11,40,42}

Blindness occurs mainly among children with birth weights below 1,000 grams at rates of 5% to 6%. Deafness, which is found in 2% to 3% of low birth weight children, does not seem to specifically affect the smallest babies.^{11,43}

The vast majority of low birth weight children are normal on neurological exams; however, the rates of neuromotor dysfunction are higher than in neurologically normal control groups. There is thus a spectrum of neurological disorders ranging from cerebral palsy to lesser and more subtle degrees of neuromotor abnormality.

Cognitive and Neuropsychological Outcomes

Low birth weight children score significantly lower on intelligence tests than do children of normal birth weight, even when sociodemographic risk factors are taken into account (see Table 2). The mean intelligence quotient (IQ) scores fall

Table 2

Comparison of Intelligence Scores of School-Age Children by Birth Weight									
Author/ Related Endnote Number*	Year of Birth	Cohort Description	Age, Years	Outcomes Measured	Birth Weight Range, grams				
Hack ⁴³	1977– 1979	Hospital	8	WISC-R** Verbal ^a		<1,500 95.7±18			≥2,500 100.6±18
Saigal ⁴⁰	1977– 1981	Regional	8	WISC-R Fullscale ^a	<1,000 91.1±6				≥2,500 103.8±12
McCormick ¹¹	1978– 1981	Multicenter very low birth weight and regional	8–10	WISC-R Fullscale ^a	<1,000 87.9±18	1,000 to 1,499 96.5±19	1,500 to 2,499 96.3±17		≥2,500 103.1±16
Teplin ³⁸	1980	Hospital	6	Kaufman MPC ^{a,b}	<1,000 86.3±14				≥2,500 96.8±11
Petersen ⁴²	1980– 1982	Hospital	4	McCarthy ^a		<1,500 101.3±18	1,500 to 2,300 109.5±12		≥2,500 116.2±12
Breslau ¹²	1983– 1985	Urban/suburban hospital	6	WISC-R Fullscale ^c		<1,500 95.8±2	1,500 to 1,999 97.8±1	2,000 to 2,499 102.3±1	≥2,500 105.2±1

^a Mean ± Standard Deviation
^b Mental Processing Composite
^c Least square means and standard error estimated in multiple regression analyses with population site, maternal IQ, maternal education, and race as covariates.
* See the related endnote numbers at the end of this article for complete citation.
** WISC-R = Wechsler Intelligence Scale for Children-Revised.

within the average range; however, the rates of deficient (IQ<70) and subnormal (IQ=70 to 84) intelligence are significantly higher than among control groups of children with normal birth weight. (See Table 3.) These differences increase with decreasing birth weight.^{11,12,38,40,43,44} Differences in IQ between low birth weight and normal birth weight groups persist even when those children with neurological abnormalities are excluded from analysis.^{12,44} Deficiencies in overall cognitive abilities are especially evident for infants weighing less than 1,000 grams (2 pounds,

Low birth weight children score significantly lower on intelligence tests than do children of normal birth weight.

3 ounces) at birth. For example, 8% to 13% of children born weighing less than 1,000 grams have subnormal intelligence,^{11,38,40} compared with 20% of those children born weighing less than 750 grams (1 pound, 10 ounces).⁴³

Evaluation of neuropsychological outcomes of low birth weight have also included assessments of specific functions, such as language abilities, memory, attention, fine and gross motor coordination, perceptual-motor skills, and nonverbal reasoning and problem solving.^{38,40,43–48}

The majority of recent studies published in the United States involving very low birth weight children show that members of this group perform more poorly than members of the full-term control group in all areas. Pervasive neuropsychological impairments are particularly pronounced in children with birth weights of less than 1,000 grams.^{38,40,49,50}

Recent findings by Hack and her colleagues suggest a relationship between the degree of low birth weight and the neuropsychological outcome.^{43,50} Extremely low birth weight children (those weighing less than 750 grams, or 1 pound, 10 ounces, at birth) performed more poorly on an extensive battery of neuropsychological tests than did infants born either at higher weights (between 750 and 1,499 grams) or at term. For several of the outcome measures, differences between the very low

Table 3

Percentage of Children with School-Age Intelligence in the Subnormal and Borderline Range by Birth Weight								
Author/ Related Endnote Number*	Year of Birth	Cohort Description	Age, Years	Birth Weight Range, grams				
Hack ⁴³	1977– 1979	Hospital	8		<1,500			≥2,500
					Percent with IQ <70 70 to 84			Percent with IQ <70 70 to 84
					6% 24%			2% 14%
McCormick ¹¹	1978– 1981	Multicenter very low birth weight and regional	8–10	<1,000	1,000 to 1,499		1,500 to 2,499	≥2,500
				Percent with IQ <70 70 to 84	Percent with IQ <70 70 to 84		Percent with IQ <70 70 to 84	Percent with IQ <70 70 to 84
				13% 29%	5% 19%		5% 17%	0% 13%
Saigal ⁴⁰	1977– 1981	Regional	8	<1,000				≥2,500
				Percent with IQ <70 70 to 84				Percent with IQ <70 70 to 84
				8% 25%				1% 4%
Teplin ³⁸	1980	Hospital	6	<1,000				≥2,500
				Percent with IQ <70 70 to 84				Percent with IQ <70 70 to 84
				18% 29%				4% 12%
Breslau ¹²	1983– 1985	Urban/sub- urban hospital	6				All <2,500	≥2,500
							Percent with IQ <70 70 to 84	Percent with IQ <70 70 to 84
							6% 23%	2% 14%

* See the related endnote numbers at the end of this article for complete citation.

birth weight infants and the term infants were twice as large as differences between the children with birth weights between 750 and 1,499 grams and the children in the full-term group. The greater frequency of medical complications associated with increasingly lower birth weights helped to account for the relatively poor outcome in the sample with birth weights below 750 grams.

Studies of neuropsychological outcomes also suggest that some cognitive skills may be more compromised than others in low birth weight children. Comparisons of neurologically intact very low birth weight children of average intelligence with full-term children in control groups point to selective impairments in areas such as mental arithmetic, visual-motor and fine motor skills, spatial abilities, expressive language, and memory.^{23,38,40,44,47,49}

Aram and colleagues failed to find evidence of specific language disorders in very low birth weight children.⁵¹ Although language disorders were more common in this group than in a geographically based sample of normal birth weight children, Aram found that these disorders were associated with general cognitive deficiency. The results of these and other studies are consistent with indications that low birth weight children show less specific impairment in verbal abilities than in perceptual-performance skills.^{50–53} The special vulnerability of low birth weight children to weaknesses in perceptual-performance skills is also consistent with evidence that early neurological insults are more closely associated with deficits in this area than with deficits in language or more general cognitive abilities.^{38,54,55} Studies focusing more specifically on neuromotor dysfunction in larger low birth weight children (those with birth weights greater than

Table 4

Behavioral Outcomes by Birth Weight								
Author/ Related Endnote Number*	Year of Birth	Cohort Description	Age, Years	Outcomes Measured	Birth Weight Range, grams			
McCormick ¹¹	1978–1981	Multicenter very low birth weight and regional	8–10	Behavior problems ^a	<1,000 29%	1,000 to 1,499 28%	1,500 to 2,499 29%	≥2,500 21%
Petersen ⁴²	1980–1982	Hospital	4	Difficulty in social behavior and few emotional resources		<1,500 28%	1,500 to 2,300 17%	≥2,500 12%

^a Clinically significant behavioral problems on National Study of Children Questionnaire
 * See the related endnote numbers at the end of this article for complete citation.

1,500 grams) are available from Europe and the United Kingdom. The findings from these studies reveal poor quality of motor function and coordination in low birth weight children. Studies also show increasing neuromotor dysfunction as birth weight decreases, even in children without evident neurological impairment.

Behavior and Social Competence

The majority of recent studies of behavior and social competence in low birth weight children pertain to very low birth weight and extremely low birth weight outcomes. Using parent and/or teacher question-

stress has been postulated but not proven.^{38,56}

The types of behavioral problems reported in low birth weight children include conduct disorder,³⁶ hyperactivity,^{56,58} and attentional weaknesses.^{57,61} Using parent and teacher behavior ratings, Szatmari and colleagues⁵⁷ diagnosed attention-deficit hyperactivity disorder (ADHD) in 16% of the children born with birth weights of less than 1,000 grams (2 pounds, 3 ounces) compared with 6.9% of the children in a matched control group. Because the groups did not differ in rates of other behavioral and emotional problems, these researchers concluded that children with birth weights of less than 1,000 grams have specific biologically based problems in attention. A pattern of shyness, unassertiveness, and withdrawn behavior has also been described.⁶¹ Parent and teacher ratings of social competence have similarly revealed that low birth weight children have more difficulty in social skills than the normal birth weight children in control groups^{36,40,43} although no differences in child temperament have been reported.⁶²

School Performance and Academic Achievement

Learning problems among low birth weight children have been documented by teacher or parent ratings of school performance and direct assessments of academic skills in clinical settings. McCormick⁵⁶ analyzed data from the National Health Interview Survey of 1981 and found an increased rate of parent-reported learning problems with decreasing birth weight (see Table 5). Additional studies have yielded similar results.^{40,60}

Researchers concluded that children with birth weights of less than 1,000 grams have specific biologically based problems in attention.

naires, these studies document an increased risk of behavioral problems^{36,42,56–58} especially among boys.^{42,59,60} McCormick⁵⁶ and Petersen⁴² found greater rates of behavioral problems with decreasing birth weight (see Table 4). Behavioral problems have mainly been described in children with cognitive deficits and neuromotor dysfunction, suggesting brain injury as a cause of these problems. Data relating behavioral problems to socioeconomic status of the family are inconsistent.^{36,60} A causal relationship between behavioral outcomes and maternal-infant separation and family

Table 5

School Performance and Academic Achievement by Birth Weight								
Author/ Related Endnote Number ^a	Year of Birth	Cohort Description	Age, Years	Outcomes Measured	Birth Weight Range, grams			
McCormick ⁵⁶	1970s	NHIS ^a	4–17	Grade repetition ^b Special education ^b School difficulty ^b		<1,500 23% 15% 34%	1,500 to 2,499 17% 5% 20%	≥2,500 11% 4% 14%
Hack ⁴³	1977– 1979	Hospital	8	Limited academic skills (reading, spelling) ^c		<1,500 34%		≥2,500 24%
Saigal ⁴⁰	1977– 1981	Regional	8	School performance Below grade level ^d Below average ^b	<1,000 39% 12%			≥2,500 17% 4%
Carran ⁶⁶	1978– 1979	Hospital	7–8	Special education ^e Mild/Moderate Severe		<1,500 20% 8%	1,500 to 2,499 11% 2%	≥2,500 13% 0%
McCormick ¹¹	1978– 1981	Multicenter very low birth weight and regional	8–10	Learning problems ^b		<1,500 25%	1,500 to 2,499 19%	≥2,500 13%

^a NHIS = National Health Interview Survey of 1981

^b Parent questionnaire

^c Tests of children

^d Teacher questionnaires

^e School records

* See the related endnote numbers at the end of this article for complete citation.

Levels of achievement in reading, spelling, and math are also lower for very low birth weight children than for full-term children.^{40,63}

Observations of a relatively high rate of learning problems in children of normal intelligence have led some researchers to speculate that low birth weight children may have specific learning disabilities. Saigal and colleagues⁴⁰ examined this issue directly by comparing the incidence of learning disabilities in a group of children having birth weights of less than 1,000 grams (2 pounds, 3 ounces) to the incidence of these problems in a matched group of full-term children.

These researchers did not find a significant difference between the groups in the rates of learning disabilities but did find that the children who weighed less than 1,000 grams at birth were more likely to be receiving special help at school. Nevertheless, neurologically intact very low birth weight children of normal intelligence score more poorly on tests of achievement than children in matched control groups.^{47,63} Based on these group comparisons, very low birth weight chil-

dren appear to be particularly vulnerable to problems in math.^{47,50}

Although most low birth weight children participate in mainstream education, rates of special education assistance are higher among these children relative to full-term groups (see Table 5). McCormick and colleagues⁵⁶ found that 34% of very low birth weight children were having school problems as defined by grade repetition or placement in special education programs. In comparison, only 14% of a group of normal birth weight children were having similar problems. The differences could not be explained on the basis of sociodemographic factors. In other studies involving very low birth weight children, rates of special education placements are reported to be closer to 50% or higher.^{63–67} A tendency for increasing rates of special education with decreasing birth weight is further substantiated in a recent study by Hack and colleagues.⁴³ Research in this area additionally suggests that rates of special education assistance may increase among low birth weight children as they progress through the grades.⁶⁶

Health Outcomes

As a group, low birth weight children experience more health problems than normal birth weight children. These problems include specific medical and surgical conditions, rehospitalization, and health-related limitations of activities of daily living.^{37,38,68–70} Adverse health outcomes increase with decreasing birth weight (see Table 6). The most common medical conditions found in low birth weight children are asthma, upper and lower respiratory infections, and ear infections. Pulmonary function tests reveal abnormalities which are considered to be secondary to either structural differences related to complications of prematurity or to familial asthma.^{71,72} Low birth weight children are rehospitalized for the above medical conditions as well as for surgeries, mainly of the eyes (strabismus), ears, nose, and throat (ear tubes, adenoids, tonsils, tracheal complications); orthopedic surgery is also performed for cerebral palsy.⁶⁹ Although respiratory infections decrease after two years of age, health problems

disease.⁷⁶ Although very little catch-up of head size occurs after one year of age, catch-up of weight and height can occur later.⁷⁴ The major determinants of catch-up growth include the duration and severity of the initial growth failure, as well as the genetic growth potential of the child as measured by parental height.

Low Birth Weight Among Children Born at Term Gestation Following Severe Intrauterine Growth Failure

Low birth weight children born at term following severe intrauterine growth failure usually weigh between 1,500 and 2,499 grams (between 3 pounds, 5 ounces and 5 pounds, 8 ounces) at birth. Prior to the 1960s, term low birth weight children were considered to have higher rates of major neurodevelopmental handicap than normal birth weight children. However, more recently, with the exception of children who have major congenital malformations or intrauterine infections (herpes, cytomegalovirus, toxoplasmosis, and the like), developmental outcomes for these children have been reported to be similar to those of their normal birth weight peers.^{77,78} This is considered to be due to improvements in perinatal care which minimize brain insult, including optimal timing of delivery, cesarean section when indicated, prevention of birth asphyxia, optimal resuscitation, and treatment of complications such as hypoglycemia and polycythemia. Extended follow-up to 9 to 11 years of age has, however, recently revealed learning deficits that were not identified prior to this age.⁷⁹ Recent literature also suggests a relationship between an abnormal intrauterine environment associated with low birth weight and adult blood pressure, cardiovascular disease, and pulmonary function.⁸⁰

Recent literature also suggests a relationship between an abnormal intrauterine environment associated with low birth weight and adult blood pressure, cardiovascular disease, and pulmonary function.

persist and contribute to excessive bed days, restricted activity, school absence, and poor school performance.^{11,37,73} Low birth weight children from disadvantaged backgrounds fare worse than socially advantaged children.⁷³

Growth

Growth attainment of low birth weight children is less than that of their normal birth weight peers.^{29,41,68,74,75} Birth-weight-related differences in mean weight, height, and head circumference increase with decreasing birth weight. Poor growth attainment is seen in both preterm and term children who are born small for age following intrauterine growth failure, and also in preterm children who have normal intrauterine growth but fail to grow after birth because of severe neonatal complications of prematurity such as chronic lung

Factors Affecting Long-Term Developmental Outcomes

Social and Environmental Factors

Social and environmental disadvantages clearly affect the long-term developmental outcomes of low birth weight children, whether measured in terms of maternal education,^{8,10,11} race,^{8,81} or social

Table 6

Health Outcomes by Birth Weight								
Author/ Related Endnote Number*	Year of Birth	Cohort Description	Age, Years	Outcomes Measured	Birth Weight Range, grams			
Overpeck ³⁷	1964–1981	NHIS ^a	<18	Three or more conditions Respiratory system conditions Central nervous system conditions Rehospitalization (two or more stays)			<2,500 12% 20% 8% 17%	≥2,500 8% 16% 4% 11%
Hack ⁶⁸	1977–1979	Hospital	8	Respiratory conditions Surgery: Number of operations 1 or more 2 or more 3 or more		<1,500 18% 37% 8% 6%		≥2,500 5% 16% 2% 0.3%
McCormick ¹¹	1978–1981	Multicenter very low birth weight and regional	8–10	Limitation in more than one activity of daily living due to health Asthma Rehospitalization Previous year	<1,000 46% 17% 6.5%	1,000 to 1,499 34% 18% 7%	1,500 to 2,499 27% 12% 5%	≥2,500 17% 11% 1.8%
Teplin ³⁸	1980	Hospital	6	Rehospitalizations	<1,000 64%			≥2,500 20%

^a NHIS = National Health Interview Survey of 1981
 * See the related endnote numbers at the end of this article for complete citation.

class.^{40,44,46,47,82–87} For most low birth weight children, social risk factors have a far greater effect on long-term cognitive outcomes than do biological risk factors. However, biological factors are more important influences on outcome for children with severe neurological insult or extremely low birth weight.^{81,84} There is also evidence that the cognitive deficits specifically associated with social or environmental risk become more pronounced over time.^{22,38,87,88}

Despite speculation that very low birth weight children are more susceptible to adverse environmental influences than are normal birth weight children,^{8,82,89} evidence in support of an exaggerated effect of social factors among very low birth weight children is scarce.⁶³ Most studies have failed to find evidence for differing long-term effects of social factors on very low birth weight infants compared with normal birth weight children.^{12,38,40,44} In fact, a few studies have observed greater differences between very low birth weight and control groups of children from more advantaged environments when compared with similar groups of children from

less advantaged environments.^{38,44} The latter findings have been interpreted as evidence that the adverse consequences of being born very low birth weight may add only minimally to the larger negative impact of environmental disadvantage. There is little doubt, however, that the combined effects of severe neonatal illness and a deprived environment can be devastating.^{47,81,83}

Biological Factors

Low birth weight is considered an index of biological risk; however, the pathophysiologic basis of risk is often unclear, especially in larger low birth weight children.⁹⁰ Medical and/or biological factors that contribute to the risk associated with low birth weight include birth defects,^{39,91} male sex,⁸⁷ birth asphyxia, and neonatal complications of prematurity including severe periventricular hemorrhage (brain damage), chronic lung disease, meningitis, seizures, hypoglycemia, and jaundice of prematurity. These complications of prematurity occur more commonly in infants with birth weights of less than 1,000 grams (2 pounds, 3 ounces), which explains why this birth weight group is at

greatest biological risk. Intrauterine growth failure in preterm very low birth weight children does not seem to contribute to poor developmental outcome over and above that resulting from prematurity and its complications. However, those with severe brain growth failure may have a poorer outcome.

Various cumulative neonatal risk scores, which include summations of most of the neonatal risk factors listed above, are also predictive of developmental outcomes of intensive care survivors. Length of hospital stay is another good predictor for neonatal morbidity because the sickest and/or smallest infants remain in the hospital for the longest periods. Subnormal

The majority of these enrichment programs have demonstrated improvements in developmental outcome.

brain growth, which is associated with the above described intrauterine and neonatal complications and which serves as a marker of severe biological insult, also correlates very well with long-term outcome.^{38,54,74,84}

Specific neuropathologic brain lesions associated with adverse low birth weight outcomes include periventricular leukomalacia and cerebral atrophy, which can result in cerebral palsy, nonspecific hypotonia, and cognitive and neuropsychological subnormality. Lesser degrees of brain damage are thought to be responsible for fine motor impairments, visuoperceptual and math difficulties, and hyperactivity.

The influence of biological genetic factors on outcomes such as intelligence and other cognitive abilities has rarely been examined in low birth weight children.^{12,86}

Enrichment Programs for Low Birth Weight Infants

Enrichment programs for low birth weight children have included neonatal in-hospital infant- and/or parent-focused programs⁹² as well as infant educational enrichment and parent support programs during infancy and early childhood.^{93,94} The majority of these programs have demonstrated improvements in developmen-

tal outcome. The Infant Health and Development Program is the largest, most recent, and comprehensive controlled trial of educational enrichment of low birth weight infants.⁹⁴ In this project, 985 infants were randomly assigned to receive either an educational curriculum focused on child development in addition to family support and pediatric follow-up or only pediatric follow-up for three years. The children who received the enrichment intervention had significantly higher mean IQ scores than did children in the control group (mean difference in IQ was 13.2 in the heavier group and 6.6 in the lighter group) and significantly fewer maternally reported behavioral problems. The gains in function were most pronounced in the domains of receptive language, visual-motor function, and special skills. The infants who benefitted most from the program were those of mothers who had high school or less than high school education, whereas children of college-educated mothers benefitted less. Thus, enrichment programs seem to be most effective among heavier low birth weight children from lower social classes who are at less severe medical risk.

Legislative Support for Early Intervention Services for Low Birth Weight Infants and Toddlers and Their Families

Research and demonstrated needs of infants and toddlers with disabilities and those at risk due to biological and/or environmental factors have contributed to the passage of federal legislation to support a range of services for young children with disabilities and their families and for those at risk for compromised development. The vast majority of low birth weight children would fall into the latter categories.

Public Law 94-142, passed in 1975, mandated services for disabled children six years of age and older. Part B of Public Law 99-457, passed in 1986, mandated services for disabled children three to five years of age, and Part H of this legislation created a family-based service model for children from birth to two years. Federal grant monies are provided to develop a coordinated, multidisciplinary system for serving the targeted populations. Inter-agency coordination councils, comprised of professionals from several disciplines

(for example, medicine, education, psychology, occupational therapy, physical therapy, and the like) in regions around the state are required to document the collaboration and coordination of multidisciplinary services. Most states have initiated services for young children with identified congenital disabilities and their families; however, much less progress has been made in serving youngsters such as low birth weight children who are vulnerable to developmental compromise because of biological or environmental risk factors.

Conclusion and Policy Recommendations

Low birth weight children represent a heterogeneous group of term and preterm infants with varying degrees of social and medical risk. Adverse outcomes include a broad spectrum of conditions ranging from normal growth and development to severe developmental abnormalities. Although the vast majority of low birth weight children function within the normal range, they have higher rates of subnormal growth, health conditions, and inferior neurodevelopmental outcomes than do normal birth weight children. Rates of abnormal outcomes increase as birth weight decreases. At school age, health problems mainly include respiratory problems such as asthma. With the exception of a small minority of children with mental retardation and/or cerebral palsy, developmental sequelae for most children include mild problems in cognition, attention, and neuromotor functioning.

The majority of recent reports of low birth weight outcomes pertain to children who have reached 8 to 10 years of age. Studies of adolescent intellectual and academic functioning of children born in the 1960s and earlier indicated that the adverse consequences of low birth weight were still apparent in adolescence. Thus, there is no reason to anticipate improvements in outcome with age in current survivors.

Social risk factors affect outcomes across the continuum of the low birth weight spectrum. Medical sequelae resulting from neonatal complications of prematurity, such as brain hemorrhage and chronic lung disease, have been identified as risk factors affecting outcomes in the low and extremely low birth weight subgroups. The physiological and biological characteristics of the pregnancy and peri-

Box 4

Policy Recommendations

1. Provide prenatal care for all to prevent prematurity to the maximum extent possible.
2. Continue perinatal research to elucidate the causes of and, thereby, to prevent prematurity and neonatal morbidity.
3. Mandate comprehensive follow-up of low birth weight children until school age. Such a mandate would include referral to early intervention services for those most in need.
4. Offer parent support and education programs to enable parents to meet the complex needs of preterm children.
5. Provide early educational experiences for very young preterm children most at risk for compromised development.
6. Intervene during the primary school years to minimize school failure.
7. Continue professional development for health care providers, educators, psychologists, and other human service providers to ensure that the multidisciplinary needs of preterm children are met to the maximum extent possible.

natal risk factors associated with the inferior outcomes of heavier low birth weight children (those weighing between 1,500 and 2,499 grams or between 3 pounds, 5 ounces and 5 pounds, 8 ounces), independent of social risk, are unclear.

Given the increasing numbers of survivors of extreme prematurity and the high health care and educational costs involved in caring for low birth weight children, it is crucial that we appreciate the full extent of any adverse outcomes, identify the children and families in greatest need of monitoring and treatment, and recognize protective factors that may assist us in designing effective interventions (see Box 4).

At present, there is a lack of solid information about the long-term follow-up of low birth weight infants in the United States. This lack of information stems not only from the difficulties in tracking families over many years, but also from the lack of a national commitment in this area. In countries that have national health care systems, it is often easier to implement long-term follow-up studies, as nationwide registration of health care users facilitates the tracking of families over the years. It is hoped that a future universal health care system in the United States will mandate documentation of the long-term outcome of low birth weight children.

There is evidence to show that enrichment programs improve the developmental outcomes for low birth weight infants. At present, there have been too few programs designed specifically to meet the special health and developmental needs of these children. Furthermore, despite enactment of federal legislation which mandated services for disabled children, enrichment programs for such disabled children are rarely available during infancy and prior to three years of age. Expanding the availability and accessibility of these enrichment programs has the potential to mediate some of the adverse developmental effects that confront low birth weight infants. Improvement of the overall educational and social environment of

families living in poverty should further influence outcomes.

Attempts to improve the long-term health and developmental outcomes of low birth weight children, apart from trying to prevent low birth weight itself, must include a commitment to research in several important areas. We need to elucidate and better understand which pregnancy and perinatal factors affect brain development, how to prevent and/or treat identified neonatal complications of prematurity; and which components of enrichment programs may best prevent and/or treat the developmental sequelae associated with both biological and social risks. This basic information will provide us with the tools to better serve the low birth weight infant.

1. Benton, A.L. Mental development of prematurely born children. *American Journal of Orthopsychiatry* (1940) 10:719–46.
2. U.S. Congress, Office of Technology Assessment. *Neonatal intensive care for low birthweight infants: Costs and effectiveness*. Health Technology Case Study 38. OTA-HCS-38. Washington, DC: OTA, 1987.
3. Hack, M., and Fanaroff, A.A. How small is too small? Considerations in evaluating the outcome of the tiny infant. *Clinics in Perinatology* (1988) 15:773–88.
4. Johnson, A., Townshend, P., Yudkin, P., et al. Functional abilities at age 4 years of children born before 29 weeks of gestation. *British Medical Journal* (1993) 306:1715–18.
5. Hack, M., Horbar, J.D., Malloy, M.H., et al. Very low birthweight outcomes of the N.I.C.H.D. Neonatal Network. *Pediatrics* (1991) 87:587–97.
6. Abramowicz, M., and Kass, E.H. Pathogenesis and prognosis of prematurity. *New England Journal of Medicine* (1966) 275:878–85.
7. Lubchenco, L.O., Horner, F.A., Reed, L.H., et al. Sequelae of premature birth: Evaluation of premature infants of low birth weights at ten years of age. *American Journal of Diseases of Children* (1963) 106:101–15.
8. Broman, S.H., Nichols, S.H., and Kennedy, W.A. *Preschool IQ: Prenatal and early developmental correlates*. Hillsdale, NJ: Lawrence Erlbaum Associates, 1975.
9. Nichols, P.L., and Chen, T. *Minimal brain dysfunction: A prospective study*. Hillsdale, NJ: Lawrence Erlbaum Associates, 1981.
10. The Infant Health and Development Program. Enhancing the outcomes of low-birth-weight, premature infants: A multisite, randomized trial. *Journal of the American Medical Association* (1990) 263:3035–42.
11. McCormick, M.C., Brooks-Gunn, J., Workman-Daniels, K., et al. The health and developmental status of very low-birth-weight children at school age. *Journal of the American Medical Association* (1992) 267:2204–8; Information in Table 6 regarding rehospitalization is contained in McCormick, M.C., Workman-Daniels, K., Brooks-Gunn, J., and Peckham, G.J. Hospitalization of very low birth weight children at school age. *Journal of Pediatrics* (1993) 122,3:360–65.
12. Breslau, N., DelDotto, J.E., Brown, G.G., et al. A gradient relationship between low birth weight and IQ at age 6 years. *Archives of Pediatric and Adolescent Medicine* (April 1994) 148:377–83.
13. Rawlings, G., Reynolds, E.O.R., Stewart, A., and Strang, L.B. Changing prognosis for infants of very-low-birthweight. *Lancet* (1971) 1:516–19.
14. Saigal, S., Rosenbaum, P., Hattersley, B., and Milner, R. Decreased disability rate among 3-year-old survivors weighing 501 to 1000 grams at birth and born to residents of a geographically defined region from 1981 to 1984 compared with 1977 to 1980. *Journal of Pediatrics* (1989) 114:839–46.

15. Shapiro, S., McCormick, M.S., Starfield, B.H., and Crawley, B. Changes in infant morbidity associated with decreases in neonatal mortality. *Pediatrics* (1983) 72:408–15.
16. Escobar, G.H., Littenberg, B., and Petitti, D.B. Outcome among surviving very low birthweight infants: A meta-analysis. *Archives of Disease in Childhood* (1991) 66:204–11.
17. McCormick, M.C. Has the prevalence of handicapped infants increased with improved survival of the very low birth weight infant? *Clinics in Perinatology* (1993) 20,1:263–77.
18. Wojtulewicz, J., Alam, A., Brasher, P., et al. Changing survival and impairment rates at 18–24 months in outborn very low-birth-weight infants: 1984–1987 versus 1980–1983. *Acta Paediatrica* (1993) 82:666–71.
19. Bhushan, V., Paneth, N., and Kiely, J.L. Impact of improved survival of very low birth weight infants on recent secular trends in the prevalence of cerebral palsy. *Pediatrics* (1993) 91:1094–1100.
20. Bregman, J., and Kimberlin, L.V.S. Developmental outcome in extremely premature infants: Impact of surfactant. *Pediatric Clinics of North America* (1993) 40,5:937–53.
21. Kiely, J.L., and Paneth, N. Follow up studies of low-birthweight infants: Suggestions for design, analysis and reporting. *Developmental Medicine and Child Neurology* (1981) 23:96–100.
22. Aylward, G.P., Pfeiffer, S.T., Wright, A., and Verhulst, S.J. Outcome studies of low birth weight infants published in the last decade: A metaanalysis. *Journal of Pediatrics* (1989) 115:515–20.
23. Ornstein, M., Ohlsson, A., Edmonds, J., and Asztalos, E. Neonatal follow-up of very low birthweight/extremely low birthweight infants to school age: A critical overview. *Acta Paediatrica Scandinavica* (1991) 80:741–48.
24. HIFI Study Group. High-frequency oscillatory ventilation compared with conventional intermittent mechanical ventilation in the treatment of respiratory failure in preterm infants: Neurodevelopmental status at 16 to 24 months of postterm age. *Journal of Pediatrics* (1990) 117:939–46.
25. Horwood, S.P., Boyle, M.H., Torrance, G.W., and Sinclair, J.C. Mortality and morbidity of 500- to 1,499-gram birth weight infants live-born to residents of a defined geographic region before and after neonatal intensive care. *Pediatrics* (1982) 69,5:613–20.
26. Hack, M., Caron, B., Rivers, A., and Fanaroff, A.A. The very low birthweight infant: The broader spectrum of morbidity during infancy and early childhood. *Journal of Developmental and Behavioral Pediatrics* (1983) 4:243–49.
27. Resnick, M.B., Bauer, C.R., Cupoli, M., et al. Florida Regional Perinatal Intensive Care program developmental evaluation component—Early developmental outcome. *Journal of the Florida Medical Association* (1983) 70,9:833–38.
28. Blackman, J.A., Lindgren, S.D., Hein, H.A., and Harper, D.C. Long-term surveillance of high-risk children. *American Journal of Diseases of Children* (1987) 141:1293–99.
29. Dunn, H.G., ed. *Sequelae of low birthweight: The Vancouver Study*. Clinics in Developmental Medicine series. London: Mac Keith, 1986.
30. Sameroff, A.J., Seifer, R., Baldwin, A., and Baldwin, C. Stability of intelligence from preschool to adolescence: The influence of social and family risk factors. *Child Development* (1993) 64:80–97.
31. Aylward, G.P., Hatcher, R.P., Stripp, B., et al. Who goes and who stays: Subject loss in a multicenter, longitudinal follow-up study. *Journal of Developmental and Behavioral Pediatrics* (1985) 6:3–8.
32. Lasky, R.E., Tyson, J.E., Rosenfeld, C.R., et al. Disappointing follow-up findings for indigent high-risk newborns. *American Journal of Diseases of Children* (1987) 141:100–105.
33. DePietro, J.A., and Allen, M.C. Estimation of gestational age: Implications for developmental research. *Child Development* (1991) 62:1184–99.
34. Landry, S.H., Chapieski, M.L., Richardson, M.A., et al. The social competence of children born prematurely: Effects of medical complications and parent behaviors. *Child Development* (1990) 61:1605–16.
35. Crnic, K.A., Greenberg, M.T., Ragozin, A.S., et al. Effects of stress and social support on mothers and premature and full-term infants. *Child Development* (1983) 54,1:209–17.
36. Ross, G., Lipper, E.G., and Auld, P.A.M. Social competence and behavior problems in premature children at school age. *Pediatrics* (1990) 86:391–97.
37. Overpeck, M.D., Moss, A.J., Hoffman, H.J., and Hendershot, G.E. A comparison of the childhood health status of normal birth weight and low birthweight infants. *Public Health Reports* (1989) 104:58–70.

38. Teplin, S.W., Burchinal, M., Johnson-Martin, N., et al. Neurodevelopmental, health, and growth status at age 6 years of children with birth weights less than 1001 grams. *Journal of Pediatrics* (1991) 118:768–77.
39. Schreuder, A.M., Veen, S., Ens-Dokkum, M.H., et al. Standardised method of follow-up assessment of preterm infants at the age of 5 years: Use of the WHO classification of impairments, disabilities and handicaps. *Paediatric and Perinatal Epidemiology* (1992) 6,3:363–80.
40. Saigal, S., Szatmari, P., Rosenbaum, P., et al. Cognitive abilities and school performance of extremely low birthweight children and matched term controls at age 8 years: A regional study. *Journal of Pediatrics* (1991) 118:751–60.
41. The Scottish Low Birthweight Group. The Scottish low birthweight study: I. Survival, growth, neuromotor and sensory impairment. *Archives of Disease in Childhood* (1992) 67:675–81.
42. Petersen, M.B., Greisen, G., Kovacs, R., et al. Status at four years of age in 280 children weighing 2,300 g or less at birth. *Danish Medical Bulletin* (1990) 37:546–52.
43. Hack, M., Taylor, G., Klein, N., and Eiben, R. Outcome of <750 gm birthweight children at school age. *New England Journal of Medicine* (1994) 331:753–59.
44. Hack, M., Breslau, N., Aram, D., et al. The effect of very low birth weight and social risk on neurocognitive abilities at school age. *Journal of Developmental and Behavioral Pediatrics* (1992) 13:412–20.
45. McDermott, S., Cokert, A.L., and McKeown, R.E. Low birthweight and risk of mild mental retardation by ages 5 and 9 to 11. *Paediatric and Perinatal Epidemiology* (1993) 7,2:195–204.
46. Crowe, T.K., Deitz, J.C., Bennett, F.C., and Tekolste, K. Preschool motor skills of children born prematurely and not diagnosed as having cerebral palsy. *Journal of Developmental and Behavioral Pediatrics* (1988) 9:189–93.
47. Hunt, J.V., Bruce, A.B., Cooper, B.A.B., and Tooley, W.H. Very low birthweight infants at 8 and 11 years of age: Role of neonatal illness and family status. *Pediatrics* (1988) 82:596–603.
48. Klein, N.K., Hack, M., and Breslau, N. Children who were very low birth weight: Developmental and academic achievement at nine years of age. *Journal of Developmental and Behavioral Pediatrics* (1989) 10:32–37.
49. Halsey, C.L., Collin, M.F., and Anderson, C.L. Extremely low birth weight children and their peers: A comparison of preschool performance. *Pediatrics* (1993) 81:807–11.
50. Taylor, H.G., Klein, N., and Hack, M. Academic functioning in <750 gm birthweight children who have normal cognitive abilities: Evidence for specific learning disabilities. *Pediatric Research* (1994) 35:289A.
51. Aram, D.M., Hack, M., Hawkins, S., et al. Very-low-birthweight children and speech and language development. *Journal of Speech and Hearing Research* (1991) 34,5:1169–79.
52. Weisglas-Kuperus, N., Baerts, W., de Graaf, M.A., et al. Hearing and language in preschool very low birthweight children. *International Journal of Pediatric Otorhinolaryngology* (1993) 26:129–40.
53. Menyuk, P., Liebergott, J., Schultz, M., et al. Patterns of early lexical and cognitive development in premature and full-term infants. *Journal of Speech and Hearing Research* (1991) 34:88–94.
54. Mutch, L., Leyland, A., and McGee, A. Patterns of neuropsychological function in a low-birthweight population. *Developmental Medicine and Child Neurology* (1993) 35:943–56.
55. Wiener, G., Rider, R.V., Oppel, W.C., and Harper, P.A. Correlates of low-birth-weight: Psychological status at eight to ten years of age. *Pediatric Research* (1968) 2:110–18.
56. McCormick, M.C., Gortmaker, S.L., and Sobol, A.M. Very low birth weight children: Behavior problems and school difficulty in a national sample. *Journal of Pediatrics* (1990) 117:687–93.
57. Szatmari, P., Saigal, S., Rosenbaum, P., et al. Psychiatric disorders at five years among children with birthweights <1000 g: A regional perspective. *Developmental Medicine and Child Neurology* (1990) 32:954–62.
58. Brandt, P., Magyary, D., Hammond, M., and Barnard, K. Learning and behavioral-emotional problems of children born preterm at second grade. *Journal of Pediatric Psychology* (1992) 17:291–311.
59. Breslau, N., Klein, N., and Allen, L. Very low birthweight: Behavioral sequelae at nine years of age. *Journal of the American Academy of Child and Adolescent Psychiatry* (1988) 27,5:605–12.
60. Sommerfelt, K., Ellertsen, B., and Markestad, T. Personality and behaviour in eight-year-old, non-handicapped children with birth weight under 1500 g. *Acta Paediatrica* (1993) 92:723–28.

61. Klein, N.K. Children who were very low birthweight: Cognitive abilities and classroom behavior at five years of age. *Journal of Special Education* (1988) 22:41–54.
62. Pfeiffer, S.I., and Aylward, G.P. Outcome for preschoolers of very low birthweight: Sociocultural and environmental influences. *Perceptual and Motor Skills* (1990) 70:1367–78.
63. Ross, G., Lipper, E.G., and Auld, P.A.M. Educational status and school-related abilities of very low birth weight premature children. *Pediatrics* (1991) 88:1125–34.
64. Hunt, J.V., Tooley, W.H., and Harvin, D. Learning disabilities in children with birthweights ≤ 1500 grams. *Seminars in Perinatology* (1982) 6:280–87.
65. Eilers, B.L., Desai, N.S., Wilson, M.A., and Cunningham, M.D. Classroom performance and social factors of children with birthweights of 1250 grams or less: Follow-up at 5 to 8 years of age. *Pediatrics* (1986) 77:203–8.
66. Carran, D.T., Scott, K.G., Shaw, K., and Beydoun, S. The relative risk of educational handicaps in two birth cohorts of normal and low birthweight disadvantaged children. *Topics in Early Childhood Special Education* (1989) 9,1:14–31.
67. Vohr, B.R., and Garcia-Coll, C.T. Neurodevelopmental and school performance of very-low-birthweight infants: A seven-year longitudinal study. *Pediatrics* (1985) 76:345–50.
68. Hack, M., Weissman, B., Breslau, N., et al. Health of very low birth weight children during their first eight years. *Journal of Pediatrics* (1993) 122:887–92.
69. McCormick, M.C., Workman-Daniels, K., Brooks-Gunn, J., and Peckham, G.J. Hospitalization of very low birth weight children at school age. *Journal of Pediatrics* (1993) 122:360–65.
70. Combs-Orme, T., Fishbein, J., Summerville, C., and Evans, M.G. Rehospitalization of very-low-birth-weight infants. *American Journal of Diseases of Children* (1988) 142:1109–13.
71. Chan, K.N., Elliman, A., Bryan, E., and Silverman, M. Respiratory symptoms in children of low birth weight. *Archives of Disease in Childhood* (1989) 64:1294–1304.
72. Mansell, A.L., Driscoll, J.M., and James, L.S. Pulmonary follow-up of moderately low birth weight infants with and without respiratory distress syndrome. *Journal of Pediatrics* (1987) 110:111–15.
73. McGauhey, P.J., Starfield, B., Alexander, C., and Ensminger, M.E. Social environment and vulnerability of low birth weight children: A social-epidemiological perspective. *Pediatrics* (1991) 88:943–53.
74. Ross, G., Lipper, E.G., and Auld, P.A.M. Growth achievement of very low birthweight premature children at school age. *Journal of Pediatrics* (1990) 117:307–12.
75. Casey, P.H., Kraemer, H.C., Bernbaum, J., et al. Growth status and growth rates of a varied sample of low birth weight, preterm infants: A longitudinal cohort from birth to three years of age. *Journal of Pediatrics* (1991) 119:599–605.
76. Hack, M., Merkatz, I.R., McGrath, S.K., et al. Catch-up growth in very low birthweight infants: Clinical correlates. *American Journal of Diseases of Children* (1984) 138:370–75.
77. Hawdon, J.M., Hey, E., Kolvin, I., and Fundudis, T. Born too small—Is outcome still affected? *Developmental Medicine and Child Neurology* (1990) 32:943–53.
78. Winer, E.K., Tejani, N.A., Atluru, V.L., et al. Four- to seven-year evaluation in two groups of small-for-gestational age infants. *American Journal of Obstetrics and Gynecology* (1982) 143:425–29.
79. Low, J.A., Handley-Derry, M.H., Burke, S.O., et al. Association of intrauterine fetal growth retardation and learning deficits at age 9 to 11 years. *American Journal of Obstetrics and Gynecology* (1992) 167:1499–1505.
80. Barker, D.J.P., ed. *The fetal and infant origins of adult disease*. London: British Medical Journal Books, 1992.
81. Cohen, S., Parmelee, A., Sigman, M., and Beckwith, L. Antecedents of school problems in children born premature. *Journal of Pediatric Psychology* (1988) 13:493–508.
82. Escalona, S.K. Babies at double hazard: Early development in infants at biologic and social risk. *Pediatrics* (1982) 70:670–76.
83. Leonard, C.H., Clyman, R.I., Picuch, R.E., et al. Effect of medical and social risk factors on outcome of prematurity and very low birth weight. *Journal of Pediatrics* (1990) 116:620–26.
84. Hack, M., Breslau, N., Weissman, B., et al. Effect of very low birthweight and subnormal head size on cognitive abilities at school age. *New England Journal of Medicine* (1991) 325:231–37.

85. Vohr, B., Garcia-Coll, C., Flanagan, P., and Oh, W. Effects of intraventricular hemorrhage and socioeconomic status on perceptual, cognitive, and neurologic status of low birth weight infants at 5 years of age. *Journal of Pediatrics* (1992) 131:280–85.
86. Aylward, G.P. The relationship between environmental risk and developmental outcome. *Journal of Developmental and Behavioral Pediatrics* (1992) 13:222–29.
87. Resnick, M.B., Stralka, K., Carter, R.L., et al. Effects of birth weight and sociodemographic variables on mental development of neonatal intensive care unit survivors. *American Journal of Obstetrics and Gynecology* (1990) 162:374–78.
88. Collin, J.F., Halsey, C.L., and Anderson, C.L. Emerging developmental sequelae in the “normal” extremely low birth weight infant. *Pediatrics* (1991) 88:115–20.
89. Sameroff, A.J., and Chandler, M.J. Reproductive risk and the continuum of caretaking casualty. In *Review of child development*. Vol. 4. F.D. Horowitz, M. Hetherington, S. Scarr-Salapatek, et al., eds. Chicago: University of Chicago Press, 1975, pp. 187–244.
90. Cohen, S.E., Sigman, M., Parmelee, A.H., and Beckwith, L. Perinatal risk and developmental outcome in preterm infants. *Seminars in Perinatology* (1982) 6:334–39.
91. McCormick, M.C. Long-term follow-up of infants discharged from neonatal intensive care units. *Journal of the American Medical Association* (1989) 261:1767–72.
92. Dudley, M., Gylter, L., Blinkhorn, S., and Barnett, B. Psychosocial interventions for very low birthweight infants: Their scope and efficacy. *Australian and New Zealand Journal of Psychiatry* (1993) 27,1:74–83.
93. Bennett, F.C. The effectiveness of early intervention for infants at increased biologic risk. In *The effectiveness of early intervention for at-risk and handicapped children*. M.J. Guralnick and F.C. Bennett, eds. Orlando, FL: Academic Press, 1987, pp. 79–114.
94. The Infant Health and Development Program. Enhancing the outcomes of low-birth-weight, premature infants. *Journal of the American Medical Association* (1990) 263:3035–42.

Primarily North American references have been included with this article. An additional list of references is available from author Maureen Hack, M.D., Department of Pediatrics, Rainbow Babies and Children's Hospital, 11100 Euclid Road, Cleveland, OH 44106.

Evidence-Based Ethics and the Care of Premature Infants

Jon Tyson

Abstract

Despite the success of newborn intensive care, a vexing ethical question remains: Which preterm infants are so malformed, sick, or immature that newborn intensive care should *not* be administered? In an attempt to answer this question, this article examines current clinical practices and the persisting effects of the controversial Baby Doe regulations. The scientific evidence for current practices is critically analyzed in relation to fundamental ethical issues for marginally viable patients of any age. A variety of strategies—some highly provocative—is proposed and discussed to facilitate better-informed, better-justified, more broadly acceptable, and more fiscally responsible ethical decisions in the care of preterm infants.

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The ongoing debate about reform of the health care system has been focused more on access and cost than on effectiveness of care. Yet, for the population as a whole, medical care appears to have only a modest effect on longevity or health.¹ Indeed, a major increase in the delivery of medical care produced almost no discernible improvement in the health status of adults during a large clinical trial to assess the benefits of providing free medical care.²

Premature infants, however, are a subgroup of the population for whom medical care has undoubted effects on outcome. As discussed elsewhere in this issue, the mortality of premature infants has decreased dramatically during the past several decades. Furthermore, the National Center for Health Statistics, which estimates total years of life lost before age 65 from a large variety of causes, has reported that the largest recent reduction in total life-years lost from any cause has occurred among premature infants.³

Despite this success, however, a vexing ethical question remains: Which premature infants are so malformed, sick, or immature that newborn intensive care (neonatal intensive care) should not be

administered? The potential benefits of intensive care—expressed in terms of total years of life or total disability-free years that may be gained from use of intensive care—are greater for these infants than for older children or adults. However, the costs—both human and material—are also greater, particularly for infants (and their families) who survive with severe life-long handicaps.

Decisions about whether to provide neonatal intensive care to marginally viable newborns are particularly difficult, in part because the infants are unable to speak for themselves. We must rely on the parents and health care professionals to make these decisions for the infants. Yet, decisions to forego or administer intensive

care involve the same fundamental ethical questions, irrespective of patient age. For this reason, advances in ethical decision making in the care of premature infants can improve ethical decisions in the care of patients of any age.

In discussing ethical problems in the care of premature infants, current practices and the controversy associated with the Baby Doe regulations are first reviewed. Then, the fundamental ethical questions about the care of these infants are analyzed in terms of the scientific evidence for current practices. Finally, based on this analysis, specific strategies are proposed to facilitate better-informed, better-justified, and more broadly acceptable ethical decisions in the care of premature infants.

Practices and Policies in the United States and Canada

Some neonatologists initiate neonatal intensive care for virtually all seriously ill, malformed, or immature infants, including infants weighing less than 500 grams (1 pound, 2 ounces) at birth or delivered before 24 weeks after the mother's last menstrual period (24 weeks gestational age). Except for infants with extremely devastating congenital anomalies (for example, anencephaly), these neonatolo-

In centers that use neonatal intensive care selectively, birth weight is often the primary criterion in deciding whether to initiate NICU care.

gists believe that prognosis cannot be adequately assessed at birth and that decisions made in the delivery room to forego neonatal intensive care result in unnecessary deaths and handicaps. Parents have little influence over the decision to begin neonatal intensive care, although they are involved in any decision to discontinue neonatal intensive care. However, these neonatologists are resistant to discontinuing neonatal intensive care.⁴ While some will agree to discontinue neonatal intensive care if the infant develops a large hemorrhage in the brain, others consider it acceptable only when death is clearly imminent.

In other centers, neonatal intensive care is used more selectively and is not initiated when the neonatologist judges that it would not be beneficial. In this situation, infants are given "comfort care"—which includes a warm environment, gentle handling, and contact with the parents as they desire—and allowed to die without administration of any painful procedures. If neonatal intensive care is initiated, the development of major complications is likely to prompt consideration of whether neonatal intensive care should be continued. Depending on the circumstances, the parents may or may not be involved in deciding to forego or initiate neonatal intensive care although they are involved in any decision to withdraw it.

In centers that use neonatal intensive care selectively, birth weight is often the primary criterion in deciding whether to initiate this care. Currently, neonatal intensive care is not routinely administered in many units to infants whose birth weight is less than 500 grams (1 pound, 2 ounces). However, for many years, the minimum birth weight at which neonatal intensive care was routinely administered was as high as 800 grams (1 pound, 11 ounces) in neonatal units in the United States. (In this article, the term "extremely premature infants" is used to refer to infants who weigh 800 grams or less—infants who, if they survive, usually are treated with a respirator for more than a month and remain in the hospital more than 100 days.⁵)

Gestational age may also be considered in decisions to administer or forego neonatal intensive care, particularly when gestational age is known with certainty and when treatment is planned prior to birth. Allen and colleagues have recently recommended starting neonatal intensive care for infants of 25 weeks gestational age or greater but not for infants of 22 weeks or less.⁶ At 23 to 24 weeks gestational age, they recommend that treatment be decided in a joint decision with the parents. These recommendations are similar to those of other U.S. and Canadian groups.⁷

In a recent survey of neonatologists,⁸ 65% of respondents indicated that they would consider parental wishes in deciding whether to initiate neonatal intensive care for an infant born at 23 to 24 weeks. If an infant born at 23 weeks gestational age deteriorated despite maximal support in the neonatal intensive care unit, 55% of the neonatologists said they would involve the parents in decision-making and

actively encourage a decision to discontinue the respirator for these infants. This percentage decreased to 48% if the infant had been born at 24 weeks and 32% if the infant had been born at 25 weeks. In a different survey,⁹ 94% of respondents recommended aggressive treatment at birth for a 625-gram infant delivered at 25 weeks; however, 53% indicated they would limit treatment if the infant developed a large intracranial hemorrhage.

Unfortunately, there is little information documenting actual practice. The proportion of infants with birth weights of 800 grams or less who received neonatal intensive care within the 12 centers of the Neonatal Research Network sponsored by the National Institutes of Child Health and Human Development has been reported.

Among infants of the same birth weight, those with the most advanced gestational age are most mature, least likely to die, and thus, most likely to benefit from neonatal intensive care. Those who are small for their gestational age (have a birth weight below the 10th percentile) fare better than infants of the same birth weight who are appropriate for their gestational age (have a birth weight in the 10th through the 90th percentile for gestational age) or large for their gestational age (have a birth weight above the 90th percentile).

Neonatal intensive care was given to approximately 55% of the smallest and most immature infants (appropriate-for-gestational-age or large-for-gestational-age infants whose birth weight was 501 to 600 grams [1 pound, 2 ounces to 1 pound, 5 ounces]). Neonatal intensive care was given to more than 80% of all remaining infants (small-for-gestational-age infants with birth weights between 501 and 800 grams [1 pound, 2 ounces and 1 pound, 11 ounces] and appropriate-for-gestational-age or large-for-gestational-age infants with birth weights between 601 and 800 grams [1 pound, 5 ounces and 1 pound, 11 ounces]).^{5,10}

However, there was considerable variation between centers. Little information about withdrawal of neonatal intensive care and the involvement of parents or ethics committees in treatment decisions is available from these or other centers.

Practices and Policies Elsewhere

European countries are apparently much less aggressive than the United States in using neonatal intensive care and place greater emphasis on assuring prenatal care to prevent premature births and on rehabilitative and social services for handicapped survivors.⁴ Recommendations not to give neonatal intensive care have been made in Denmark for infants whose gestational age is below 25 or 26 weeks¹¹ and in Sweden for infants whose birth weight is below 600 grams.¹² In Australia, neonatal intensive care is typically not recommended below 25 weeks gestational age or 650 grams (1 pound, 7 ounces) birth weight; depending on the desires of the

European countries are apparently much less aggressive than the United States in using neonatal intensive care.

parents, neonatal intensive care may not be administered up to 800 grams (1 pound, 11 ounces) birth weight or 27 weeks gestational age.¹³ In less-well-developed countries, neonatal intensive care, if available at all, may be available only to infants weighing at least 1,000 grams (2 pounds, 3 ounces)¹⁴ or more.¹⁵

Outside North America, parents of premature infants tend to have a more passive role or no role at all in treatment decisions for premature infants.^{12,14} Moreover, opposition to the involvement of ethics committees has been documented in a variety of countries.^{12,14}

The Baby Doe Regulations in the United States: A Controversial and Uncertain Legacy

Under the Baby Doe regulations of 1984,¹⁶ withholding neonatal intensive care on the basis of handicap—or, in the case of extremely premature infants, increased risk of handicap—was deemed to be discrimination and a violation of the Rehabilitation Act of 1973. Threatened by loss of federal funds, hospitals were required to post signs providing the phone number of a “Baby Doe Hotline” to report non-

treatment. Such reports were to be immediately investigated by "Baby Doe Squads" that interrogated physicians, nurses, and other personnel and reviewed confidential hospital records. A storm of protest ensued. These regulations were struck down in 1986 by the U.S. Supreme Court on the grounds that the autonomy of the states had been violated and that the Rehabilitation Act did not apply to the medical care of handicapped infants.

In the interim, Congress passed the Child Abuse and Treatment Act of 1984 (Public Law 98-457)—often referred to as the revised Baby Doe regulations—that defined the withholding of "medically indicated" treatment as child abuse and neglect, rather than discrimination. State child protective service agencies were held responsible for determining when appropriate treatment had been unduly withheld. The act asserted that such treatment may be withheld only when (1) the infant is chronically and irreversibly comatose, (2) treatment would be "futile" and "merely prolong dying," or (3) treatment would be *both* "virtually futile in terms of survival of the infant" and "inhumane."

"Law has failed medicine with respect to intensive care decisions by creating two conflicting legal standards."

The terms "futile," "virtually futile," and "inhumane" were only vaguely defined, a fact that makes the act difficult to interpret in clinical practice. Whether "virtually futile" is narrowly interpreted (for example, a 0.1% or 1% chance of survival) or more liberally interpreted (for example, a 5% chance of survival) makes considerable difference.

Ironically, this act discriminates against handicapped newborns by denying them the legal right accorded to all other incompetent patients to refuse treatment through surrogates.¹⁷ This and other ethical objections to the act have been of little concern to commentators who dismiss the law as largely symbolic and of little import to neonatal care. However, others¹⁸ are deeply disturbed by this act and fear that even a small possibility of the reprisals for its violation—including loss of hospital privileges by the physician and loss of federal funding by the hospital and

state agency—may have serious and unrecognized consequences.¹⁷

To explore the effect of the act on clinical practice, Kopelman and colleagues surveyed neonatologists in the United States.¹⁹ Among the 494 respondents, 66% felt the act had reduced parental rights to consent to or refuse treatment based on the infant's best interests; 60% felt that the act did not allow adequate consideration of suffering; and 56% felt that infants were overtreated when survival was very unlikely. An additional 11% to 15% were uncertain about such issues.

The neonatologists were asked whether the use of a respirator should be continued for a 550-gram premature infant who had developed seizures and a large hemorrhage in the brain. The estimated chance of survival was 5% with almost no chance of survival without severe handicap. Thirty percent of the neonatologists felt that the law *required* use of the respirator; an additional 18% were uncertain; and 68% noted that the act had changed their approach to such infants. When asked about an infant who had severe hydrocephalus (spinal fluid obstruction causing marked distention of the brain and head), infection within the brain, and blindness, 77% of the neonatologists felt that treatment was not in the infant's best interest; yet, 47% felt that the act required treatment even against the parents' wishes.

Although the act's legal standing has been questioned, its effects appear to be exactly those intended by its proponents—diminished parental autonomy, reduced consideration of infant suffering and future quality of life, and expanded use of neonatal intensive care for handicapped or immature infants. At the same time, funding has been restricted or reduced for follow-up programs, rehabilitative care of handicapped infants, and pediatric programs of undisputed benefit, including immunization programs. Moreover, other federal regulations (for example, the Patient Self-Determination Act) have been enacted to protect and promote—not to reduce—the autonomy of patients or their surrogates in decisions to administer or forego intensive care. Considering the highly complex issues involved in treatment decisions for handicapped or extremely premature infants, the Baby Doe regulations can be viewed as a simplistic governmental effort to control a very difficult and important area of medical care

and ethical decision making. These regulations were implemented without demonstrating broad societal support, a consistent or coherent rationale, or a manifest commitment to improving the long-term outcome of immature or handicapped survivors.

To date, the act has not been interpreted at the appellate level and has not been directly challenged.²⁰ However, Clark has recently reported that the standards of the act have not been applied in legal cases involving withdrawal of care.

Under the state laws applied to these cases, quality-of-life consideration is encouraged, and parental permission for neonatal intensive care is ordinarily required; parental decisions are subject to external review only if the infant's caregivers consider the parental decision to be unreasonable; and the physician who continues treatment without obtaining a court order after both parents have withdrawn their consent may be committing battery.

In contrasting the federal standards under the act with those under the emerging standards of state law, Clark contends that "law has failed medicine with respect to intensive care decisions by creating two conflicting legal standards" and that "physicians must choose which of the two standards to utilize and take their chances"²⁰

What Care Is Ethical?

Legal questions aside, what care should be given to the most immature, malformed, or sick premature infants? The important relevant ethical principles include preservation of life, alleviation of suffering, non-maleficence ("do no harm"), patient autonomy, and justice (fair allocation of medical resources).²¹ When ethical problems arise in the care of premature infants, there is usually conflict between two or more of these principles. How best to address the conflict between these abstract principles while dealing with the concrete problems of premature infants has been debated for years. The eight major questions discussed below are of fundamental importance in addressing the ethical questions involved in using intensive care for patients of any age.

What Outcomes Are Too Dismal to Justify Aggressive Care?

Without neonatal intensive care, virtually all extremely ill, malformed, or immature infants die within a few hours, if not a few minutes, after birth. Yet, neonatal inten-

sive care can make the outcome worse—death occurring after days or weeks of suffering. Moreover, some, though not many, survivors have severe lifelong handicaps considered to be worse than death by many parents.²² Thus, neonatal intensive

"Just as the interests of the infant limit parental authority, so the interests of the family limit what can be required of the family for the sake of the infant."

care is not necessarily beneficial or justified simply because it affords a modest chance of survival.

Most religious leaders, ethicists, physicians, and members of the lay public agree that a variety of factors beside the risk of dying should be considered in deciding how to treat marginally viable patients. Contrary to the Baby Doe regulations, these factors include pain and suffering, future quality of life, and sometimes the cost of care.^{4,23,24}

Should the Effect on the Family Be Considered?

The effect of neonatal treatment decisions on the family are considered to be irrelevant under the Baby Doe regulations; however, this view has not gone unchallenged.^{25–27} Strong asserts that the principle of non-maleficence should be applied to the effect of treatment decisions on the family as well as the infant. "Just as the interests of the infant limit parental authority, so the interests of the family limit what can be required of the family for the sake of the infant."²⁶ Silverman argues for balancing the interests of the infant, the family, and society, noting that "parents of a badly damaged baby often resent the implied demand that their family is required to pass a 'sacrifice test' to satisfy the moral expectations of those who do not have to live, day by day, with the consequences of diffuse idealism. It is easy, some parents say, to demand prolongation of each and every new life that requires none of one's own . . . resources to maintain that life later."²⁵

Will Aggressive Care Improve or Worsen the Outcome?

Unfortunately, the effect of intensive care on the outcome of marginally viable premature infants is not easily predicted. This

problem results in part from uncertainty about gestational age. A one- or two-week error can change whether neonatal intensive care is considered to be justified. Yet, the error is often several weeks or more whether gestational age is estimated from the infant's physical examination or the mother's menstrual history.^{28,29} Many mothers of premature infants have little or no prenatal care, irregular menstrual cycles, or an uncertain menstrual history which makes the determination of an exact gestational age difficult.³⁰

The effect of neonatal intensive care on outcome is also not well predicted from birth weight. Outcome is best predicted using multiple factors—birth weight, gestational age, gender, and condition at birth. However, even when all of these factors were used, it was impossible to predict with great accuracy whether infants whose birth weights were less than 800 grams (1 pound, 11 ounces) would survive or die when given neonatal intensive care.⁵

Severe handicap is also difficult to predict. The use of sonography has been a major advance in identifying brain damage. Yet, such damage is often not detectable on sonograms until after decisions to administer, forego, or withdraw mechanical ventilation must be made. Moreover, the relation of clinical findings in the neonatal period to long-term outcome is often not clear in the results from the available follow-up studies.

The Need for Rigorous Follow-Up Studies

It is difficult to assess the relationship between neonatal events and longer-term outcomes because it is difficult to conduct valid follow-up studies. This problem results, in part, because follow-up evaluation and home care have been woefully underfunded. Informed ethical decision making requires an understanding of all important consequences to the infant and family which might result from decisions to administer or forego neonatal intensive care. Yet, few follow-up studies have included families of infants who died, and no follow-up study has related the long-term outcome of the family to the decisions made to administer or forego neonatal intensive care to the infant. This lack of information is a fundamental problem for ethical decision making in the care of newborn infants.²⁵

What Care Is Mandatory?

Should intensive care be routinely administered because outcome cannot be well predicted? Some believe that intensive care is obligatory unless it has been shown to be futile. However, futility is a meaningful and unambiguous term only when quantitatively defined.^{31,32} As recommended by one group, intensive care would be considered futile only when the likelihood of treatment failure had been shown to be at least 97%.³¹ This approach appears to be plausible. Yet, at least for neonatal intensive care, futility is virtually impossible to demonstrate.

Futility—An Unattainable and Unsatisfactory Criterion

Hospitals vary in the outcomes that can be achieved. Thus, a neonatologist cannot use results from other hospitals to demonstrate futility in his or her own hospital. To show that neonatal intensive care is futile for preventing death among infants with a birth weight of less than, say, 500 grams (1 pound, 2 ounces), it would be necessary to administer neonatal intensive care to at least 100 such infants.³¹ Moreover, because the birth of these very tiny infants is so rare, it would require five or more years in almost all U.S. hospitals to complete such a study. Many of the parents might not agree to neonatal intensive care, and serious ethical objections might be raised by any of a variety of people. Moreover, the neonatologist could not be confident that the likelihood of death was at least 97% unless *all* 100 of the infants had such an outcome.³¹ Even then, such certainty might not be warranted because of ongoing improvements in obstetric or neonatal care.

If even one infant survived, neonatal intensive care would be considered to be mandatory under the above approach. The suffering of all the infants who died (as well as the costs of their care) would be ignored. Use of a more stringent requirement for futility (for example, demonstration that the likelihood of death is at least 99%) would be even more problematic. Use of a less stringent definition (for example, a 95% likelihood of death or severe handicap) would still pose major problems and mandate care that might produce much more harm than good.

Evidence-Based Ethics and Medical Reasonableness

Under the usual rules of evidence in medicine, the only mandatory interventions are those for which there is credible evidence that the benefits outweigh the hazards and burdens.³³ Evidence-based decision making^{34,35} allows consideration of the level of care that is reasonable, based on the quality of evidence available; the identified benefits, hazards, and costs of treatment; and as is crucial in a pluralistic society, the values and preferences of the patient or surrogate.³⁶ Thus, medical reasonableness is a more broadly acceptable criterion than is futility for deciding whether to forego or administer neonatal intensive care.

What Care Is Optional? What Care Is Investigational?

The concept that neonatal intensive care may be an ethically optional therapy for some infants has been widely discussed. Little attention has been focused on whether neonatal intensive care in some circumstances should be considered an

Neonatal intensive care should be considered to be an investigational therapy for infants for whom its benefits are highly uncertain.

investigational therapy, a therapy for which the value is sufficiently uncertain that there should be special care to obtain consent and to evaluate its effects. In an evidence-based approach to ethical decision making, neonatal intensive care should be considered to be an investigational therapy for infants for whom its benefits are highly uncertain. Whether a traditional institutional review board or some other body should oversee the use of neonatal intensive care as an investigational therapy should be carefully considered.

For both optional and investigational use, the neonatologist and the parents should jointly decide whether to administer neonatal intensive care. However, when neonatal intensive care is used as investigational therapy, parents should be clearly informed that neonatal intensive care has dubious value and should explicitly consent to its use, and to the extent feasible, it should be provided—as for organ transplantation^{37,38}—only in carefully selected units. In the author's view, these units should have (1) exemplary neonatal outcomes documented for high-risk infants born in their center, (2) carefully standardized follow-up evaluations through at least 18 months of age with no more than a 20% loss to follow-up at that age among infants for whom intensive care was optional or investigational, and (3) sufficient resources to provide investigative neonatal intensive care without compromising outcome for infants for whom neonatal intensive care is mandatory or optional. Success in publishing clinical research in peer-reviewed journals would also be highly desirable.

What Cost Is Too High?

Unfortunately, the costs as well as the benefits must be considered in the use of neonatal intensive care. While some people find it abhorrent to consider these costs, expenditures to preserve life are limited throughout our society. For example, we limit what we spend to purchase safer automobiles, build safer roads, and enforce traffic safety laws. (Indeed, highway speed limits were increased despite the predictable increase in traffic deaths as well as costs.) In proclaiming the importance of medical care, physicians sometimes lose sight of the opportunity costs of medicine—the lost opportunities to devote the same resources to improve education, employment, housing, or other social goods. Silverman notes, “It is easy to see how senseless it would be to send a fully staffed neonatal intensive care unit to rescue very small or severely malformed neonates to an impoverished country like Ethiopia. But we also need to see the folly of ignoring the disparity...between unlimited medical life-prolongation in the days

and the severity of the handicaps in those survivors.⁴⁰

If two medical programs result in the same expenses and the same number of life-years gained, the program that results in the fewest handicapped survivors will have the lowest cost per quality-adjusted life-year gained. Because a goal of medicine is to maximize the quality as well as the length of life, this program could be considered to have greater utility for the cost. The use of quality-adjusted life-years for this purpose is similar to that of “well-years” or of “disability-adjusted life-years” (DALYs), a measure recently hailed as a major advance in assessing the global burden of different diseases.⁴¹

However, the use of quality-adjusted life-years is not without controversy or problems. Such use has been criticized for discriminating unfairly against the disabled. However, use of a measure like quality-adjusted life-years which favors therapies that prevent handicap would seem to have no inherent conflict with concern for the welfare of handicapped persons. However, it is difficult to know how to adjust appropriately for disability and disease, in part because quality of life in the presence of handicaps and chronic illnesses may be rated higher by those affected than by other persons.⁴²

It is also not clear that a life-year should be valued the same for all persons, for example, the old versus the young; persons who are responsible for only themselves versus pregnant women or persons responsible for young children, elderly parents, or a disabled spouse.

In defining priorities for Medicaid expenditures, an attempt was made in Oregon to use a measure comparable to quality-adjusted life-years to rank medical and surgical therapies. This ranking was abandoned, partly because of sharp criticism of inconsistent or irrational results.⁴³ Such results were at least partly due to inadequate information to properly rank different therapies.

In the revised and less controversial Oregon ranking, clear priority was given to the care of pregnant women and children. Seventeen categories of care were ranked according to their importance. The rankings were defined by using scientific data, political importance, and other unspecified criteria. Within categories, therapies were ranked according to perceived effectiveness. Maternity care and

For both optional and investigational use, the neonatologist and the parents should jointly decide whether to administer neonatal intensive care.

and weeks immediately after birth and, later, the total lack of supporting care of vulnerable, often unwanted infants living in unsanitary housing amidst the social chaos of violence and crime in inner city slums.”³⁹

Assessing Medical Costs Relative to Their Value

To aid in deciding how to use limited health care resources, costs should be expressed relative to some measure of value.⁴⁰ The cost-effectiveness of neonatal intensive care can be expressed as the cost per extra survivor who would have died without neonatal intensive care or as the cost per additional life-year gained by survivors who would have died without neonatal intensive care. Assessments of the cost utility of neonatal intensive care can be expressed as the cost per quality-adjusted life-year (QALY) gained as a result of neonatal intensive care. In such assessments, the number of life-years gained from intensive care is reduced according to the number of handicapped survivors

care of the newborn—including low birth weight infants—were ranked second only to the category of life-saving therapies which result in full recovery. However, it remains to be determined whether our society as a whole would choose to accord a higher priority for newborn infants and pregnant women than for other citizens and, if so, whether this would be on the basis of an equal or higher value per life-year or quality-adjusted life-year gained.

The Ratio of Cost to Value: Better for Intensive Care of Premature Infants Than for Adults?

A fundamental problem in comparing the costs of care for different interventions or different patients in the United States is that hospital charges are designed to maximize revenues and are an unreliable indicator of true costs. The most comprehensive assessment of the short- and long-term costs of neonatal intensive care comes from a Canadian study.⁴⁴ This information is the basis for official estimates of the cost of neonatal intensive care in the United States.⁴⁵

For at least the great majority of premature infants, this study suggests that the cost of neonatal intensive care is not excessive relative to its utility. Indeed, the estimated cost per quality-adjusted life-year gained for infants with birth weights of 1,000 to 1,500 grams (2 pounds, 3 ounces to 3 pounds, 5 ounces) was \$4,500, less than that for treating severe or even mild hypertension in 40-year-old males (\$9,400 to \$19,100).⁴⁶ Cost increased with decreasing birth weight. Yet, the estimated cost per quality-adjusted life-year gained for infants with birth weights of 500 to 1,000 grams (1 pound, 2 ounces to 2 pounds, 3 ounces) was \$31,800, still less than the estimates for coronary artery bypass surgery (\$36,300) or renal dialysis (\$47,100 to \$54,000).

With advances in neonatal intensive care since this study, the cost utility is likely to have improved for infants whose birth weight exceeds 800 to 900 grams (1 pound, 11 ounces to 2 pounds, 0 ounces). However, cost per quality-adjusted life-year gained for smaller infants is uncertain and may have increased substantially. New comprehensive economic analyses are needed. Nevertheless, analyses of hospital stays performed using data from the Neonatal Research Network⁵ suggest that the cost per life-year gained or per quality-adjusted life-year gained from intensive care may still be less—perhaps much less—for most infants with birth weights of 501 to

800 grams (1 pound, 2 ounces to 1 pound, 11 ounces) than for many adults. Hospital charges for intensive care of adults expressed per life-year gained at home were recently reported to be \$181,308 for the highest-risk elderly patients,⁴⁷ \$95,142 for adults with solid tumors, and \$449,544 for adults with hematologic cancers.⁴⁸ Total costs may be even higher for resuscitative

Analyses of hospital stays suggest that the cost per life-year gained may still be less—perhaps much less—for most infants with birth weights of 501 to 800 grams than for many adults.

efforts of adults outside the hospital who do not initially respond⁴⁹ and such programs as cholesterol screening in young adults.⁵⁰

Is Rationing of Care at the Bedside an Unavoidable Reality?

Findings like those noted above indicate the importance of better assessing the true costs of expensive medical therapies and defining societal priorities for expensive medical care for patients of all ages. It is also important that physicians use the available resources wisely. Two reports have noted a worsening outcome among infants with birth weights greater than 1,000 grams (2 pounds, 3 ounces) as use of neonatal intensive care for infants with birth weights between 500 and 1,000 grams (1 pound, 2 ounces and 2 pounds, 3 ounces) increased.^{51,52} Even in the United States, inadequate resources for neonatal intensive care may now be or may soon become a serious unrecognized problem.^{52,53} Stringent measures to reduce costs are now being implemented in many neonatal units, and pressure to ration is intensifying throughout the health care system.^{52,53} The often-repeated dogma that rationing should not occur at the bedside ignores the clinical realities of busy intensive care units with limited beds, staff, or support services.^{54–56} To minimize preventable deaths and handicaps, resources must be used in the most effective manner feasible.

Who Should Decide?

A conceptual analysis of the role that society, parents, and physicians should play in making treatment decisions for neonatal intensive care is shown in Table 1 (based

Table 1

A Proposal for Use of Newborn Intensive Care for Premature or Other High-Risk Infants			
Care Category* Based on Societal Judgment	Societal Judgment of Cost Relative to Value	Parental Involvement in Decision Making	Rights of Infants and Parents; Duties of Physicians and Society
Unreasonable	Unacceptable	No	Newborns/parents have no right to newborn intensive care (NIC), and physicians/society ought not offer it.
Investigational	Possibly acceptable	Yes	Diversion of limited resources may be justified if NIC is provided in a manner such that burden/benefit ratio is assessed. Parents have a right to elect NIC for their newborn contingent upon their consent that therapy is provided under these conditions. Physicians/society ought to provide such therapy only under these conditions.
Optional	Probably acceptable	Yes	Parents have a right to elect/decline NIC for their newborn. Physicians/society have a duty to inform parents regarding benefits and burdens.
Mandatory	Acceptable	No	Parents have no right to decline NIC for their newborn. Physicians/society have a duty to provide NIC.
* Provided that adequate resources are available in a neonatal unit where the infant could receive intensive care.			

Source: Fleck, L., Lorenz, J., and Tyson, J. Developing guidelines for clinical and public policy. Unpublished manuscript.

on the work of Fleck, Lorenz, and Tyson⁵⁷). In principle, the designation of neonatal intensive care as unreasonable, investigational, optional, or mandatory

The designation of neonatal intensive care as unreasonable, investigational, optional, or mandatory should be a societal judgment based on the best available evidence concerning the benefits and the cost.

should be a societal judgment based on a painstaking analysis of the best available evidence concerning the benefits and the cost. Describing the steps that would constitute an appropriate process to achieve a societal judgment is beyond the scope of this article; however, the process would necessarily involve a broad variety of persons, including neonatologists, parents, economists, policy analysts, and members of the lay public.

When Parents Should *Not* Be Involved

Neonatal intensive care would be mandatory (last category in Table 1) when the cost is judged to be acceptable and the evidence of benefit is strong, as for a 1,500-gram infant born at 31 weeks gestational age with respiratory distress syndrome in the United States. In this situation, the parents do not participate in decision making; they have no right to demand that neonatal intensive care be withheld, and the physician is obligated to administer neonatal intensive care. (If the resources within the hospital are not adequate, the infant should be transferred to an appropriate facility whenever feasible.) Neonatal intensive care would be unreasonable (first category in Table 1) when there is little or no evidence that it would be beneficial and when the expected value of that care would not justify the costs. Barring major advances in neonatal intensive care, care of this type would be unreasonable for an infant weighing 250 grams (0 pounds, 9 ounces) born at 20 weeks gestational age with a slow heart rate. In this situation,⁵⁸ parents would not participate in decision making and would have no right to de-

mand neonatal intensive care, and physicians ought not to administer neonatal intensive care.

When Parents Should Be Involved

As indicated in Table 1, parents have a right to be involved in decision making whenever neonatal intensive care is optional or investigational. The neonatologist needs the freedom to initiate neonatal intensive care if the parents need more time to participate effectively in treatment decisions. However, well-prepared parents may be able to participate in decision making at or before birth. In an important article, Harrison²⁷ has urged the development and evaluation of new strategies to improve decision making, including the use of advance directives written during pregnancy to advise physicians of parental preferences if the appropriateness of resuscitation or aggressive treatment at birth is questioned.

Classification of Infants

How should infants be classified into the different categories? Any specific clinical criteria (birth weight, gestational age, and so on) would have to be periodically revised as neonatal care and prognosis changed. However, this problem might be avoided by developing criteria based on specific levels of risk for the occurrence of either death or severe neonatal morbidity. (Severe neonatal morbidity among infants with birth weights under 1,500 grams [3 pounds, 5 ounces] might be defined as Grade III or IV intracranial hemorrhage; cystic white matter disease; necrotizing enterocolitis requiring surgery; and a need for oxygen therapy at 36 weeks postmenstrual age. These disorders are associated with a prolonged need for intensive care and painful procedures or complications.)^{5,27,59}

Neonatologists are likely to differ considerably in the risk levels that they would select to classify individual babies.⁶⁰ As noted above, a societal judgment needs to be made. However, for the sake of discussion, the author's view is that the initiation of neonatal intensive care might be considered mandatory when the risk of death or severe neonatal morbidity (estimated as described below) is 50% or less, optional when the risk is 51% to 75%, and investigational when the risk is 76% to 95%. Neonatal intensive care might be considered unreasonable when the risk is greater than 95% (with the possible exception of infants who are born in centers that are

qualified to give investigational neonatal intensive care and whose attending neonatologist and parents desire to initiate such therapy). These risk levels refer to those for infants born in centers with neonatal intensive care units.

Large numbers of infants are required to develop precise estimates of risk for a given birth weight, gestational age, and sex. However, outcome data are published periodically from the Neonatal Research Network⁶¹ and the Vermont-Oxford Trials Network.⁶² (Neonatologists working in large neonatal units could use data for infants in their unit during the previous three to five years.) If recent Network data

Parents have a right to be involved in decision-making whenever neonatal intensive care is optional or investigational.

were used, the initiation of neonatal intensive care might be designated as investigational for small-for-gestational-age females with birth weights below 500 grams (1 pound, 2 ounces), and appropriate for both small-for-gestational-age males with birth weights below 700 grams (1 pound, 8 1/2 ounces), and all other infants with birth weights below 600 grams (1 pound, 5 ounces). Similarly, initiation of neonatal intensive care could be considered as mandatory for small-for-gestational-age females with birth weights above 700 grams and appropriate for both small-for-gestational-age males with birth weights above 900 grams and all other infants with birth weights above 800 grams. After neonatal intensive care is initiated, the infant's risk would change depending on his condition, response to therapy, and age. Thus, separate criteria would need to be developed for decisions to withdraw neonatal intensive care at various ages after it has been started.⁶³

The Uncertain Role of Hospital Bioethics Committees

The number and influence of hospital bioethics committees appears to have increased considerably after the Child Abuse and Treatment Act. These committees may reduce the likelihood of hasty or unreasonable decisions. They may also be very useful as advisory bodies to address ethical questions raised by clinical staff or disagreement between parents and physi-

cians. However, these committees pose important potential problems, including the possibility that the members might not know enough about the patient or the

The best way to further the autonomy of the parents as well as the welfare of the infant is to increase what is known about the benefits and hazards of neonatal treatment methods and regimens.

medical problem, or might be biased by institutional concerns.^{64,65} These committees will require further evaluation before their proper role is clear. There seems to be no information to indicate that they should routinely review or participate in treatment decisions for high-risk newborns.

Seeking Consent in the Early Neonatal Period

The goal of informing and involving parents appropriately in treatment decisions is of indisputable importance. Yet, this goal is often difficult to achieve, particularly during labor or shortly after delivery when decisions to forego or initiate neonatal intensive care are often made. If the baby was transported to a neonatal intensive care unit, the parents may be unavailable because they live in a distant community. Moreover, fathers are often not immediately available. About half of the mothers of infants weighing less than 1,500 grams (3 pounds, 5 ounces) at birth have undergone a cesarean section. Many of these mothers have major illnesses or complications. Most receive potent medications. Virtually all experience considerable physical and emotional distress. Moreover, as discussed below, "adequately" or "fully" informed consent may be impossible even if the parents—who are often young or poorly educated—are told everything known by the physician.⁶⁶

Use of Unproven Therapies: A Common and Unavoidable Dilemma

Many widely used therapies in neonatology have unproven value. Even such basic and necessary treatment decisions as how and when to feed the infant, how much

oxygen to administer, and when to administer blood involve highly complex issues that no one adequately understands. Unproven therapies and treatment regimens are used commonly in all areas of medicine.⁶⁷ However, as discussed below, premature infants are particularly vulnerable to unanticipated but potentially devastating treatment hazards.⁶⁸ The use of unproven therapies and treatment regimens remains a fundamental and inadequately appreciated issue in the ethics of caring for premature infants.

How Can We Better Serve Our Patients in Using Unproven Therapies?

The best way to further the autonomy of the parents as well as the welfare of the infant is to increase what is known about the benefits and hazards of neonatal treatment methods and regimens.

A Pressing Need for Clinical Trials

Uncertainty about the value of a therapy is most likely to be resolved by conducting a randomized controlled clinical trial—a study in which chance determines which patients receive alternative therapies or treatment methods. Other kinds of studies are a notorious source of misleading information, unjustified treatment recommendations, and widespread harm to patients. While it may be very difficult to assess treatment benefits even in randomized trials, therapies that have not been tested in such trials may be considered to have unproven value.

The resistance to clinical trials voiced by some ethicists and philosophers reflects a misunderstanding of statistics and of clinical realities.^{69,70} Indeed, ethical considerations should encourage—not discourage—the performance of properly controlled trials when the best therapy is unknown.^{68–71} A controlled trial of an unproven therapy is clearly preferable to hazardous clinical use of the same therapy. Unproven therapies are typically prescribed in clinical practice without any independent monitoring, without consent, and with little, if any, effort to inform the parents of what is known and not known about the therapy. In clinical trials, a much more serious effort is made to inform the patient (or surrogate).

This information must be provided verbally and in writing, and consent obtained using a form approved by the investigator's institutional review board. The use and effects of unproven therapies in

randomized trials—in contrast to clinical practice—are scrutinized by funding agencies, institutional review boards, data safety and monitoring committees, peer-reviewers, and readers of the published report.

At the very least, these safeguards assure that the physician conducting a clinical trial is highly motivated to use an unproven therapy in the safest, most effective manner possible based on a careful assessment of the best available information. The findings of the trial will foster wide clinical use of this therapy if benefit is shown. If, however, the “therapy” proves to be ineffective or harmful, the number of patients treated with this agent will be minimized, an important ethical advantage of clinical trials.

The Double Standard for Informed Consent in Clinical Practice and Clinical Trials: A Need for Reform

Smithells has quipped, “I need permission to give a new drug to half my patients but not to them all.”⁷² This double standard of more stringent requirements and regulation of consent in research than in clinical practice encourages widespread use of therapies before they have been properly tested. Yet, with the safeguards noted above, patient autonomy and welfare are better protected in clinical trials than in clinical practice. Despite the notorious and inexcusable abuses that have sometimes occurred in research,⁷³ the number of patients harmed by the use of unproven therapies in clinical practice is likely to be orders of magnitude greater than the number harmed in clinical trials.⁷⁴ In neonatology, for example, well-meaning use of poorly tested regimens of oxygen and antibiotics resulted in death or handicap for thousands of babies over a period of several decades.⁶⁸

A growing number of ethicists and physicians have called for equal standards of consent for use of unproven therapies in clinical practice and research.^{75,76} Such a standard should be based on the development of better methods to meet the needs and wants of our patients,⁷⁴ methods that are more sensitive to the wide differences among parents in their background, education, and values, their desire to receive information and to participate in treatment decisions, and their ability to cope under extremely difficult circumstances.

Summary and Recommendations

Treatment decisions for extremely premature infants involve highly complex medical and ethical issues. However well meaning, the imposition of ostensibly simple rules for decision making—such as

Increased support for clinical trials is needed to increase the recognition and use of therapeutic advances and to reduce the number of patients who receive well-intended “therapies” that, in fact, are ineffective or even harmful.

those promulgated under the Baby Doe regulations—may only increase the suffering of the infant and the family and the devastating long-term effects of perinatal tragedy.

The following kinds of strategies are recommended to policymakers to help improve ethical decision making in the care of high-risk newborns:

1. *Increase support for programs and research needed to augment the scientific basis for treatment decisions.* As discussed above, follow-up programs are particularly important but very difficult to conduct and woefully underfunded. Increased support for clinical trials is needed to increase the recognition and use of therapeutic advances and to reduce the number of patients who receive well-intended “therapies” that, in fact, are ineffective or even harmful. Clinical trials should be considered a critical public health need.

2. *Increase the support for programs and research needed to augment the ethical basis for treatment decisions.* Considerable research is needed to define better ways to meet the wants and needs of distraught parents in the perinatal period. We need to develop and evaluate better strategies to inform different parents about their infant’s condition and treatment and to involve them in decisions to use unproven methods of treatment. As discussed above, the double standard for consent in clinical practice and research encourages widespread use of unproven therapies without proper testing. This should be recognized as a serious problem, and alternative approaches should be formally evaluated.

3. *Address the cost of neonatal intensive care by strategies that will also augment the ethical and scientific quality of neonatal intensive care.* These strategies include more appropriate involvement of parents in treatment decisions, recognition of neonatal intensive care as an investigative therapy for some infants, and identification of neonatal units that achieve exemplary outcomes and research. Serious consideration should be given to funding neonatal intensive care as investigative therapy only for infants born in or transferred to these

grams or interventions relative to the goals of medicine. As noted above, current hospital accounting systems do not allow an accurate measure of true cost. Better mechanisms to assess cost are crucial to making intelligent choices in funding expensive medical programs. Moreover, considerable research is needed to relate the true costs to the benefits, whether these are expressed in life-years gained, quality-adjusted life-years gained, or a better measure yet to be developed.

Serious consideration should be given to funding neonatal intensive care as investigative therapy only for infants born in or transferred to these units.

units. Rather than provide funding for routine clinical use of therapies that have not been shown to be effective in clinical trials, serious consideration should also be given to funding their use only in clinical trials. At least initially, this approach might be politically feasible only for new therapies. However, over the long term, it might be a highly effective method to improve outcome as well as reduce cost.

4. *Support efforts to provide better estimates of the cost and value of all major medical pro-*

5. *Promote efforts to define the goals of medicine more clearly at a societal level.* This has been a critical but neglected issue in the current health care debate.^{77,78} The proper use of limited public funding for health care will depend on both the value ascribed by society to medical care (relative to other societal goods) and the relative value ascribed to the prevention and treatment of suffering, the prevention and rehabilitation of disability, and the postponement of death. These are crucial issues, of course, for patients of all ages.

A cooperative effort among parents, clinicians, clinical investigators, and policymakers is needed to make full use of strategies like those suggested above. This effort will augment the ethical and scientific quality of treatment decisions for premature infants, decisions that have profound long-term consequences for these infants and their families.

1. Aday, L.A., Begley, C.E., Lairson, D.R., and Slater, C.H. *Evaluating the medical care system: Effectiveness, efficiency, and equity.* Ann Arbor, MI: Health Administration Press, 1993, p. 53.
2. Brook, R.H., Ware, J.E., Rogers, W.H., et al. Does free care improve adults' health? Results from a randomized controlled trial. *New England Journal of Medicine* (1983) 309:1426-34.
3. Centers for Disease Control and Prevention. Years of potential life lost before age 65: United States, 1990 and 1991. *Journal of the American Medical Association* (1993) 269:2842.
4. Young, E.W.D., and Stevenson, D.K. Limiting treatment for extremely premature, low-birth-weight infants (500-750 g). *American Journal of Diseases of Children* (1990) 144:549-52.
5. Tyson, J., Younes, N., Verter, J., and Wright, L. Viability, severe morbidity, and resource needs associated with intensive care of newborns 501-800 g birth weight. Unpublished.
6. Allen, M.C., Donohue, P.K., and Dusman, A.E. The limit of viability—Neonatal outcome of infants born at 22 to 25 weeks' gestation. *New England Journal of Medicine* (1993) 329:1597-601.
7. Hack, M., and Fanaroff, A.A. Outcomes of extremely immature infants—A perinatal dilemma. *New England Journal of Medicine* (1993) 329:1649-50.
8. Sanders, M., Donohue, P.K., Oberdorf, M.A., et al. Perceptions of viability: Parental role in medical decision-making. *Pediatric Research* (1993) 33:29A.
9. Wolder, B.W., Driscoll, J.M., and Fleischman, A.R. "If there's a chance . . .": Decision strategy for premature neonates—A national survey. *Pediatric Research* (1993) 33:29A.

10. Tyson, J., Wright, E., and Wright, L. Is futility a valid basis to withhold intensive care among newborns 501–800 grams birth weight? Presentation to the Society for Pediatric Research. Baltimore, MD. May 1992.
11. Consensus statement from the Danish Medical Research Council and the Danish Hospital Institute. Extremely preterm infants. *International Journal of Technology Assessment in Health Care* (1992) 8:548–50.
12. Levin, B.W. International perspectives on treatment choice in neonatal intensive care units. *Social Science and Medicine* (1990) 30:901–12.
13. Buchanan, N. The very-low-birthweight infant: Medical, ethical, legal, and economic considerations. *Medical Journal of Australia* (1987) 147:184–87.
14. Wainer, S., and Khuzwayo, H. Attitudes of mothers, doctors, and nurses toward neonatal intensive care in a developing society. *Pediatrics* (1993) 6:1171–75.
15. Renzong, Q. Economics and medical decision-making: A Chinese perspective. *Seminars in Perinatology* (1987) 11:262–63.
16. U.S. Department of Health and Human Services. Nondiscrimination on the basis of handicap relating to health care for handicapped infants. *Federal Register* (1984) 49:1622–54.
17. Angell, M. The Baby Doe rules. *New England Journal of Medicine* (1986) 314,10:642–44.
18. Moskop, J.C., and Saldanha, R.L. The Baby Doe rule: Still a threat. *Hastings Center Report* (1986) 16:8–12.
19. Kopelman, L.M., Irons, T.G., and Kopelman, A.E. Neonatologists judge the “Baby Doe” regulations. *New England Journal of Medicine* (1988) 318:677–83.
20. Clark, F.I. Intensive care treatment decisions: The roots of our confusion. *Pediatrics* (1994) 94:98–101.
21. Ruark, J.E., and Raffin, T.A. Initiating and withdrawing life support. *New England Journal of Medicine* (1988) 318:25–30.
22. Torrance, G.W., Boyle, G.W., and Harwood, S.P. Application of multi-attribute utility theory to measure social preferences for health states. *Operations Research* (1982) 30:1043–69.
23. Kraybill, E. Parental autonomy in situations of moral ambiguity. *Journal of Pediatrics* (1988) 113:327.
24. Arras, J.D. Quality of life in neonatal ethics: Beyond denial and evasion. In *Contemporary issues in fetal and neonatal medicine, Vol. 3: Ethical issues at the outset of life*. W.M. Weil and M. Benjamin, eds. Boston: Blackwell Scientific Publications, 1987, pp. 151–86.
25. Silverman, W. Overtreatment of neonates? A personal retrospective. *Pediatrics* (1992) 90:971–76.
26. Strong, C. The neonatologist’s duty to patient and parents. *Hastings Center Report* (August 1984) 14,4:10–16.
27. Harrison, H. Principles for family-centered neonatal care. *Pediatrics* (1993) 92:643–50.
28. Ballard, J.L., Khoury, J.C., Wedig, K., et al. New Ballard score, expanded to include extremely premature infants. *Journal of Pediatrics* (1991) 119:417–23.
29. Kramer, M.S., McClean, F.H., Boyd, M.E., and Usher, R.H. The validity of gestational age estimation by menstrual dating in term, preterm, and postterm gestations. *Journal of the American Medical Association* (1988) 260:3306–8.
30. Tyson, J., Guzik, D., Rosenfeld, C.R., et al. Prenatal care and cohort analyses. *Pediatrics* (1990) 85:195–204.
31. Schneiderman, L., Jecker, N., and Jonsen, A. Medical futility: Its meaning and ethical implications. *Annals of Internal Medicine* (1990) 112:949–54.
32. Lantos, J.D., Singer, P.A., Walker, R.M., et al. The illusion of futility in clinical practice. *American Journal of Medicine* (1989) 87:81–84.
33. Sackett, D.L., Haynes, R.B., Guyatt, G.H., and Tugwell, P. *Clinical epidemiology: A basic science for clinical medicine*. Boston: Little, Brown, 1991, pp. 193–223, 283–301.
34. Mike, V. Ethics, evidence, and uncertainty. *Controlled Clinical Trials* (1990) 11:153–56.
35. Evidence-Based Medicine Working Group. Evidence-based medicine: A new approach to teaching the practice of medicine. *Journal of the American Medical Association* (1992) 268:2420–25.
36. Englehardt, H.T. Bioethics in pluralist societies. *Perspectives in Biology and Medicine* (1982) 26:64–78.

37. Moore, F.D. The desperate case: CARE (costs, applicability, research, ethics). *Journal of the American Medical Association* (1989) 261:1483–84.
38. Hosenpud, J.D., Breen, T.J., Edwards, E.B., et al. The effect of transplant center volume on cardiac transplant outcome. *Journal of the American Medical Association* (1994) 271:1844–49.
39. Silverman, W.A. Setting a limit in the treatment of neonates: All or none? In *The very low birthweight infant*. G. Duc, A. Huch, and R. Huch, eds. New York: Georg Thieme, 1990, pp. 111–28.
40. Drummond, M.F., Stoddart, G.L., and Torrance, G.W. *Methods for the economic evaluation of health care programmes*. New York: Oxford University Press, 1992.
41. Foege, W.H. Preventive medicine and public health. *Journal of the American Medical Association* (1993) 270:251–52.
42. Patterson, D.R., Miller-Perrin, C., McCormick, T.R., and Hudson, L.D. When life support is questioned early in the care of patients with cervical-level quadriplegia. *New England Journal of Medicine* (1993) 328:506–9.
43. Hadorn, D.C. Setting health care priorities in Oregon: Cost effectiveness meets the rule of rescue. *Journal of the American Medical Association* (1991) 265:2218–25.
44. Boyle, M.H., Torrance, G.W., Sinclair, J.C., and Harwood, S.P. Economic evaluation of neonatal intensive care of very-low-birth-weight infants. *New England Journal of Medicine* (1983) 308:1330–37.
45. U.S. Congress, Office of Technology Assessment. *Neonatal intensive care for low birthweight infants: Costs and effectiveness*. Health Technology Case Study 38. OTA-HCS-38. Washington, DC: OTA, 1987.
46. Torrance, G.W., and Zipursky, A. Cost effectiveness of antepartum prevention of Rh immunization. *Clinics in Perinatology* (1984) 11:267–80.
47. Cohen, I.L., Lambrinos, J., and Fein, A. Mechanical ventilation for the elderly patient in intensive care: Incremental charges and benefits. *Journal of the American Medical Association* (1993) 269:1025–29.
48. Schapira, D.V., Studnicki, J., Bradham, D.D., et al. Intensive care, survival, and expense of treating critically ill cancer patients. *Journal of the American Medical Association* (1993) 269:783–86.
49. Gray, W.A. Prehospital resuscitation: The good, the bad, and the futile. *Journal of the American Medical Association* (1993) 270:1471–72.
50. Hulley, S.B., Newman, T.B., Grady, D., et al. Should we be measuring blood cholesterol levels in young adults? *Journal of the American Medical Association* (1993) 269:1416–19.
51. Doyle, L.W., Murton, L.J., and Kitchen, W.H. Mortality with increasing assisted ventilation of very-low-birth-weight infants. *American Journal of Diseases of Children* (1989) 143:223–27.
52. Tyson, J., Perlman, J., Rosenfeld, C., and Arencibia-Mireles, O. Resource limitations: A major ethical issue in the care of indigent infants <1500 g birth weight? *Pediatric Research* (1992) 31:26A.
53. Eddy, D.M. Health system reform: Will controlling costs require rationing services? *Journal of the American Medical Association* (1994) 272:324–28.
54. Kalb, P.E., and Miller, D.H. Utilization strategies for intensive care units. *Journal of the American Medical Association* (1989) 261:2389–95.
55. Engelhardt, H.T., and Rie, M.A. Intensive care units, scarce resources, and conflicting principles of justice. *Journal of the American Medical Association* (1986) 255:1159–62.
56. Society of Critical Care Medicine Ethics Committee. Consensus statement on the triage of critically ill patients. *Journal of the American Medical Association* (1994) 271:1200–1203.
57. Fleck, L., Lorenz, J., and Tyson, J. Developing guidelines for clinical and public policy. Unpublished manuscript.
58. Pellegrino, E.D. Ethics. *Journal of the American Medical Association* (1993) 270:202–3.
59. Anand, K.J., and Hickey, P.R. Pain and its effects in the human neonate and fetus. *New England Journal of Medicine* (1987) 317,21:1321–29.
60. Lantos, J.D., Tyson, J.E., Allen, A.A., et al. Withholding and withdrawing life-sustaining treatment in neonatal intensive care: Issues for the 1990s. *Archives of Diseases in Childhood*. In press.

61. Hack, M., Horbar, J.D., Malloy, M.H., et al. Very low birth weight outcomes of the National Institute of Child Health and Human Development Neonatal Network. *Pediatrics* (1991) 87:587–97.
62. Investigators of the Vermont-Oxford Trials Network Database Project. The Vermont-Oxford Trials Network: Very low birth weight outcomes for 1990. *Pediatrics* (1993) 91:540–45.
63. Tyson, J., Wright, E., Malloy, M., and Wright, L. How predictable is the outcome and care of ventilated extremely low birth weight infants? Presentation to the Society for Pediatric Research. New Orleans, LA. 1991.
64. Lo, B. Behind closed doors: Promises and pitfalls of ethics committees. *New England Journal of Medicine* (1987) 317:46–50.
65. Siegler, M. Ethics committees: Decisions by bureaucracy. *Hastings Center Report* (June 1986) 16,3:22–24.
66. Silverman, W. The myth of informed consent: In clinical practice and in clinical trials. *Journal of Medical Ethics* (1989) 15:8–11.
67. Roper, W.L., Winkenwerder, W., Hackbarth, G.M., and Krakauer, H. Effectiveness in health care: An initiative to evaluate and improve medical practice. *New England Journal of Medicine* (1988) 319:1197–1202.
68. Silverman, W. Human experimentation in perinatology. *Clinics in Perinatology* (1987) 14:403–16.
69. Mike, V. Philosophers assess randomized clinical trials: The need for dialogue. *Controlled Clinical Trials* (1989) 10:244–53.
70. Freedman, B.F. Equipoise and the ethics of clinical research. *New England Journal of Medicine* (1987) 317:141–45.
71. Roy, D.J. Controlled clinical trials: An ethical imperative. *Journal of Chronic Diseases* (1986) 39:159–62.
72. Smithells, R. Iatrogenic hazards and their effects. *Postgraduate Medicine* (1975) 51,(Suppl. 2):39–52.
73. Rothman, D.J. Ethics and human experimentation: Henry Beecher revisited. *New England Journal of Medicine* (1987) 317:1195–99.
74. Tyson, J. Dubious distinctions between research and clinical practice using experimental therapies: Have our patients been well served? In *Ethics and perinatology: Issues and perspectives*. A. Goldworth, W.A. Silverman, D.K. Stevenson, and E.W.E. Young, eds. Oxford: Oxford University Press. In press.
75. King, J. Informed consent. *Institute of Medical Ethics Bulletin* (1986) Suppl. 3:2–19.
76. Chalmers, T., Frank, C., and Reitman, D. Minimizing the three stages of publication bias. *Journal of the American Medical Association* (1990) 263:1392–95.
77. Gaylin, W. Faulty diagnosis: Why Clinton's health care plan won't cure what ails us. *Harper's Magazine*. October 1993, pp. 57–64.
78. Callahan, D. Our fear of dying: How our determination to control mortality has distorted the mission of medicine. *Newsweek*. October 4, 1993, p. 67.

Unintentional Injuries

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Unintentional injuries, or injuries that occur without specific intent of harm, are a leading cause of death and disability for children in the United States. Each year, approximately 3,600 children die, 20,000 children become permanently disabled, 550,000 children are hospitalized, and 15 million children visit the emergency room because of unintentional injuries.^{1,2} The implications of these injuries for children and their families are large. Consequences can include time lost from school, decreased ability to participate in normal activities, or early loss of life.

Fortunately, many childhood unintentional injuries are preventable using fairly simple strategies that have been proven to work.³ Understanding sources of injury data and how they fit in a larger context is necessary for implementing and evaluating any prevention program. This Child Indicators defines unintentional injuries and discusses sources of information on mortality and morbidity resulting from them. It also considers issues surrounding interpretation of unintentional injury data, specifically for motor vehicle crashes, the leading cause of death for young children in this country.

Defining Unintentional Injuries

Unintentional injuries include only those injuries that occur without intent of harm. Such injuries are frequently called accidents or accidental in common usage. However, increas-

ingly the term accident is regarded as a misnomer for unintentional injuries because it suggests unpredictability or a lack of control over the circumstances surrounding an event. The National Center for Injury Prevention and Control at the Centers for Disease Control and Prevention does not use the term accident at all because this term promotes the idea that injuries cannot be prevented when, in fact, the likelihood of many childhood injuries can be reduced using relatively simple strategies.

Unintentional injuries generally stem from interaction between a child's developmental stage, a parent's or supervising adult's understanding (or lack of understanding) of the child's abilities and vulnerability, and a product or environmental circumstance.⁴ For example, a parent who places a toddler at the top of a stairway with no barrier is not properly compensating for the child's lack of stair-climbing ability with a safety barrier. If the child should fall down the

stairs and be injured, the circumstance of being at the top of the stairs with no barrier, the child's lack of climbing ability, and the parent's misunderstanding of appropriate settings for the child all contribute to the probability of the fall. Although the fall might be classified as an accident and the subsequent injuries might be termed unintentional, the probability of both events could have been greatly reduced by several different interventions.

There is no official classification scheme distinguishing intentional from unintentional injuries; however, Box 1 shows injuries typically included in the intentional and unintentional categories. Because the classification stems from intent instead of consequence, it can be difficult to distinguish unintentional injuries from intentional ones. This is particularly true for young children, who cannot always communicate the circumstances of their injuries. The clearest cases of unintentional

injury are those obviously not intended to occur. Most motor vehicle crashes, for example, are clearly unintentional, although some adolescent motor vehicle crashes may represent intentional, self-destructive behavior. Other events leading to injuries may sometimes be considered intentional but can be unintended, such as self-inflicted poisonings or gunshot injuries from firearm use, particularly among very young children. Purposely inflicted injuries such as child abuse and neglect are usually considered intentional because the abuser intended to hurt the child even if the degree of harm was not foreseen.

The distinction between intentional and unintentional is more of a continuum than a dichotomy. Take, for example, the child injured by falling down a flight of stairs. The physical consequences of the injury are clear, but the circumstances surrounding it may not be. The child may have fallen because there was no protective barrier or railing. In that instance, the injury would likely be classified as being caused by an unintentional fall. Or an adult or another child may have inadvertently pushed the child down the stairs, in which case the proper injury category might be unclear. Alternatively, the child may have been pushed down the stairs by an abusive parent, which would result in an intentional injury. The end result of each event for the child's physical health is the same, but strategies for preventing the injury would be different in each scenario.

Correctly classifying the causes of injuries is essential for the design of preventive measures. Fortunately, the intent of the injury is clear in the

majority of cases.⁵ However, in some instances, determining this information may be difficult.⁶ Child abuse and other intentional injuries can be hard to categorize. For this reason, estimates of the number of children suffering these types of injuries may be low. A recent analysis suggested that annually about 85% of child deaths from child abuse or neglect are misclassified as being from unintentional injuries.⁷ While not all injury researchers agree with the magnitude of this finding, the potential for misclassification is clear.⁵

Mortality Data

Because data on mortality are collected for the whole nation on a regular basis, they are the most readily available and frequently used source for measuring the impact of injuries on children. The most common source of mortality data is the U.S. vital statistics system which uses information from death certificates to keep track of the cause of every death in the United States. Data are collected at the local level, usually by counties or cities. Each local area has a count of the number of deaths due to specific causes which occur within its borders annually. Each year, the states collect data from the counties on births and deaths following the reporting requirements of the federal government and send computer files containing the data to the National Center for Health Statistics (NCHS). The data are compiled by NCHS, and annual reports are published discussing the number and causes of deaths in a given year by age group and other demographic categories.

Vital statistics death records use external cause of injury classification codes, or E codes, to categorize injuries

along with standard cause of death classifications. The standard mortality classifications, called N codes, document the effects of an injury and the part of the body injured but do not explain how it happened. For example, a death resulting from a motor vehicle crash might be called a head injury in N codes, while in E codes it would be described as a "motor vehicle accident." The E codes provide a crucial link between the cause of an injury and its effects, which is very helpful in injury prevention planning. Use of E codes on death certificates is required for all deaths that are injury related.

Most deaths from external causes must be investigated by state coroners or medical examiners. The cause of death recorded on the death certificate for injuries is most often determined by the coroner or medical examiner, depending on the state where the death occurred and the circumstances surrounding the death. Coroners are generally elected to office and usually have no formal medical training, while medical examiners are appointed to office and are required to be physicians in 49 states. This difference in personnel introduces some variation and inconsistency in the coding of the cause of death. In addition, the death certificate form itself varies somewhat from state to state. However, the cause of death portion does not vary extensively. Some states have instructions and examples right on the form and others do not, and the number of blank lines provided varies. The National Center for Health Statistics provides states with recommended death certificates, instruction manuals for coroners and medical examiners, and

Box 1

Categorizing Injuries

Unintentional Injuries

Injuries due to motor vehicles
 to occupants
 to pedestrians
 to bicyclists
 Bicycle injuries
 Boating injuries
 Choking and suffocation
 Falls
 Drowning
 Near-drowning
 Fires and burns
 Unintentional firearm injury
 Unintentional poisoning
 Occupational injuries
 Farm injuries
 Sports injuries
 Injuries due to toys and recreational equipment
 Any other injury that was not intended

Intentional Injuries

Homicide
 Suicide
 Rape
 Assault and battery
 Domestic violence
 Child abuse and neglect
 Any other injury caused on purpose

- The categories presented here are not official, but are those in common usage in injury prevention.
- Unintentional injuries, as defined here, occur far more often than intentional injuries.
- Motor vehicle injuries are the most common serious injury for children.

Source: Adapted from Children's Safety Network. *A data book on child and adolescent injury*. Washington, DC: National Center for Education in Maternal and Child Health, 1991.

sample legislation for state vital statistics acts but does not require the states to use them.⁸

As shown in Figure 1, vital statistics can be helpful in determining the types of unintentional injuries that are important for children, especially when E codes are used. According to vital statistics, 40% of all deaths for children ages 1 to 14 are due to "accidents and adverse effects," and nearly half of those involve motor vehicles.⁹ (Even though the Centers for Disease Control and Prevention prefers the term injury, vital statistics uses the term accidents in its record keeping for historical reasons.) Vital statistics tabulates deaths from homicide and suicide separately from "accidents and adverse effects" and distinguishes unintentional injuries by using categories such as "accident caused by handgun" and "accidental drowning and submersion." However, as previously discussed, it is some-

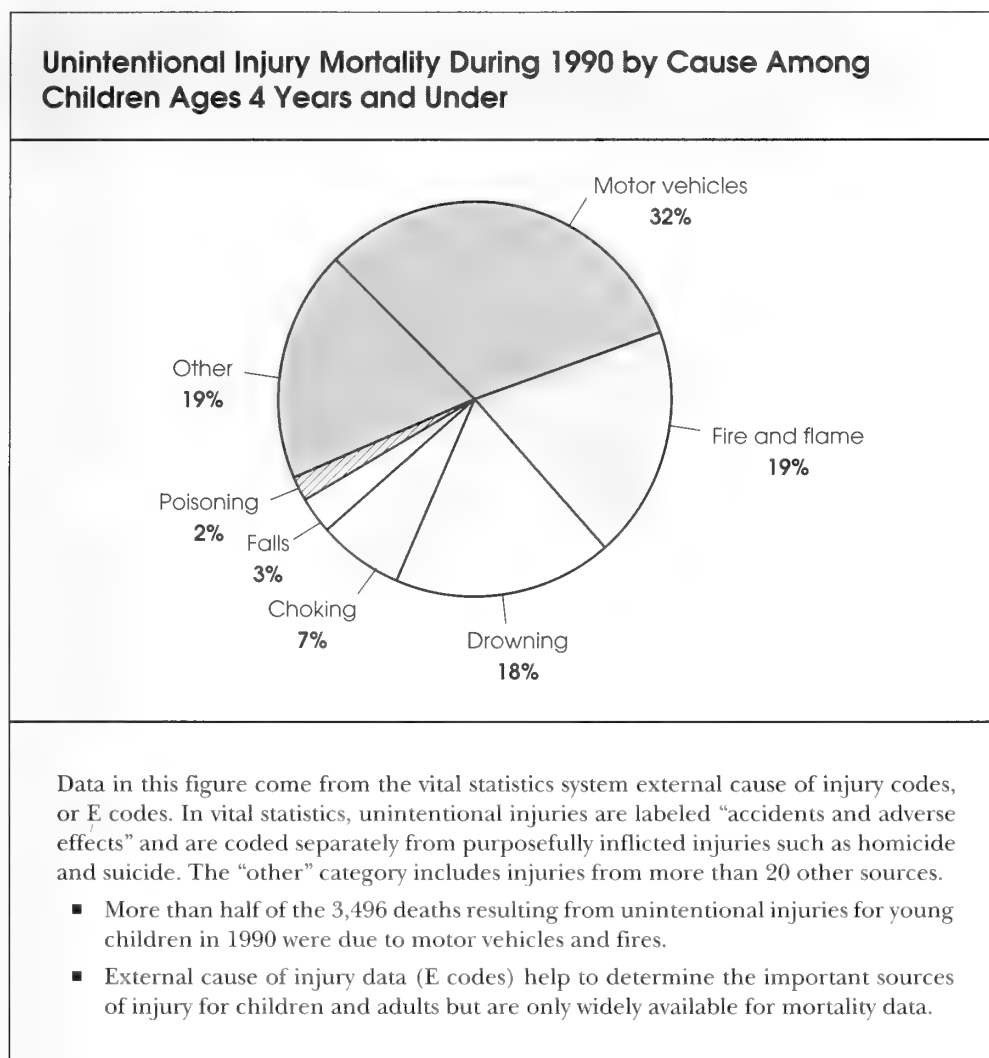
times difficult to know if the reported deaths are truly unintentional. Some portion of the deaths coded as "accidents" are likely to be from intentional injuries. Even with these difficulties, mortality is an important outcome of some types of unintentional injuries, and there is much to be learned from available mortality data.

The vital statistics system is not the only source of injury mortality data. Other, more specialized sources exist, such as the Fatal Accident Reporting System (FARS) kept by the National Highway Traffic Safety Administration (NHTSA). The NHTSA contracts with state agencies to provide information on fatal crashes in a standard format. FARS tracks motor vehicle crashes in which one or more participants died within 30 days of the crash and collects information on specific aspects of each crash, including seat belt and child safety seat use.¹⁰ The FARS system,

designed to monitor and help improve highway safety, captures a detailed picture of each fatal crash, which allows tracking of items such as restraint use that are not collected in vital statistics.

Data on fatalities do not account for important nonfatal outcomes of unintentional injuries, such as short- or long-term disability or time lost from school. Considering mortality data without data on nonfatal injuries can lead to ignoring injuries that can have a great effect on children's lives and their use of health care services. For example, sports injuries are a very common childhood occurrence and are a major contributor to long-term health problems and increased use of the medical care system by children. If mortality data are considered alone, sports injuries will not be seen as an important health problem because the number of deaths from sports injuries is

Figure 1



Source: Unpublished data from the Mortality Branch of the National Center for Health Statistics, Washington, DC.

low. Another limitation of mortality data is that they may demonstrate regional variations which have more to do with the quality or availability of trauma care than with the actual number or severity of injuries. Rural areas, for instance, may have higher unintentional injury mortality than urban areas because, other things being equal, areas with readily available trauma care will have lower mortality than those without trauma facilities nearby.¹¹

Morbidity Data

Morbidity data, which measure sickness and disability, are another indicator of the effects of unintentional injury on chil-

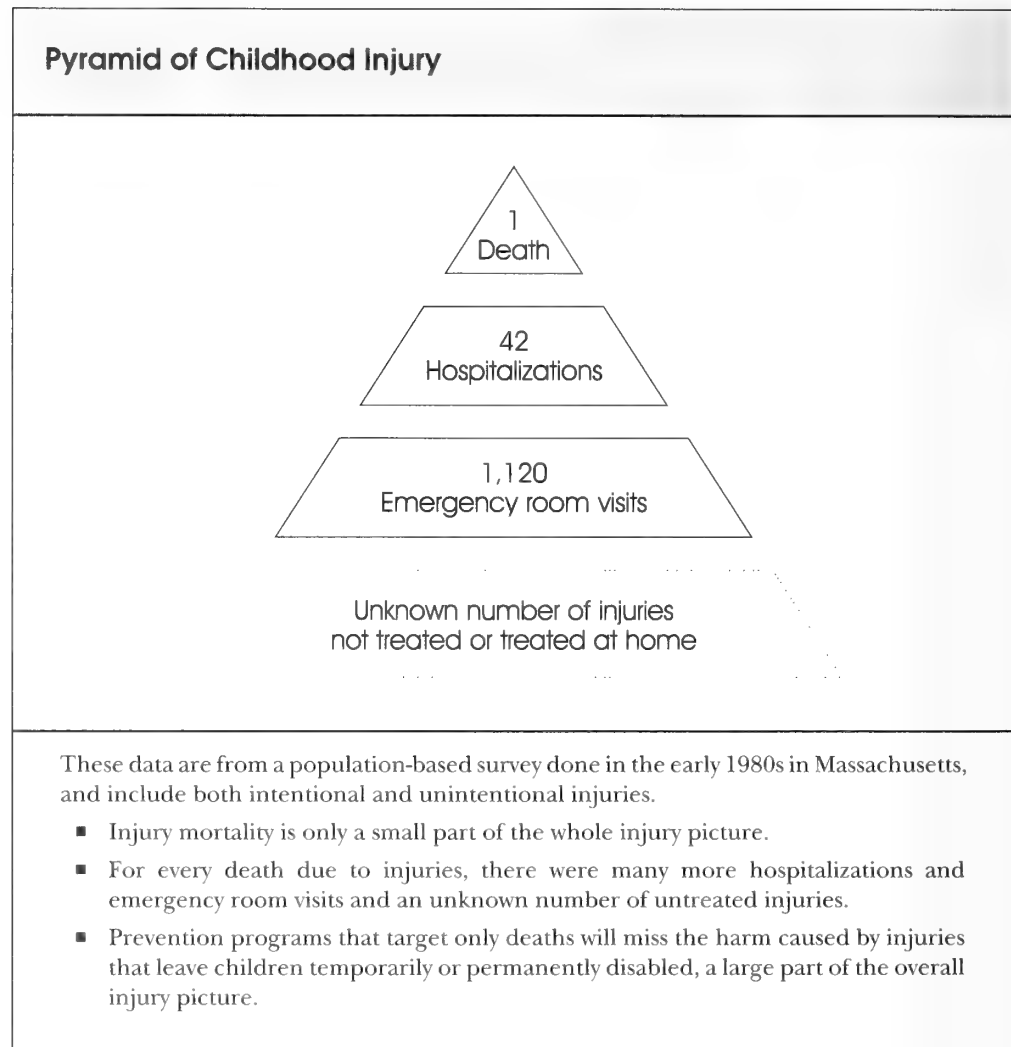
dren, but these data are not as readily available as mortality data. One of the more recent population-based studies of unintentional injuries was done in Massachusetts in 1980 and 1981.¹² Data were collected during one year from hospital discharge records in 14 cities and towns. Hospital data collectors recorded all injury cases that resulted in hospital admission or death and sampled emergency room visits for injuries. These morbidity data show the magnitude of the effects of injuries other than death.

As is shown in Figure 2, for every single death due to unintentional injuries among the Massachusetts children, there were 42 hospitalizations, and

1,120 emergency room visits. Another more recent population-based study of children enrolled in a northwestern health maintenance organization (HMO) recorded no deaths from injuries for more than a one-year period but 247 medically treated injuries per 1,000 children age 19 and under.¹³ Millions more children receive care for their injuries in physicians' offices or in outpatient clinics.¹ The base of the pyramid is probably the largest piece of all—those injuries that do not involve the medical care system but are, instead, treated at home or not treated at all.

National data on the outcomes of injuries, rehabilitation, and long-term disability

Figure 2



Source: Children's Safety Network. *A data book on child and adolescent injury*. Washington, DC: National Center for Education in Maternal and Child Health, 1991, p. 13, Figure 2.7.

are generally not available.^{11,14} The best data available come from hospital discharge abstracts, which contain detailed information, including diagnosis, on patients who were admitted to the hospital, but these data are state-based and are, therefore, not uniformly collected across the country. Hospitals in several states are required to collect information on the external causes of injuries (E codes, such as those shown in Figure 1) for discharge or billing records, but partly because these data are not necessary for reimbursement, collection is not widespread.^{15,16}

An additional problem with injury data on morbidity is that there is no reporting

mechanism for care received in an ambulatory setting, so children who incur injuries and are not admitted to the hospital are not routinely counted. Laws requiring child care centers to report injuries vary from state to state, but even when the data are collected, they are not often used for prevention planning.¹⁷

Measuring the Effectiveness of Prevention Strategies

Data on injury mortality and morbidity can help identify sources of injury which warrant intervention. When a preven-

tion program is implemented, available morbidity and mortality data can often be helpful in measuring the overall effect of the program. Sometimes, though, measurement of effectiveness with available, standard data sources is difficult. Vital statistics mortality data alone, for example, may give a misleading impression of the effects of laws requiring use of child safety seats in reducing deaths from motor vehicle crashes, which are the leading cause of death for young children. Other, more specifically relevant data must be introduced to understand the whole picture.

Because car seats were shown to be effective in preventing injuries and fatalities

in young children, between 1978 and 1985, all 50 states implemented laws that required small children to ride in car seats when in a motor vehicle.^{18,19} In the following years, the use of child restraints in cars, including child safety seats, increased, as measured by the Occupant Protection Survey (OPS), which monitored restraint use in 19 cities from 1983 to 1990.²⁰ For infants, restraint use grew from 66% in 1984 to 83% in 1990, and for toddlers, it increased from 44% in 1984 to 84% in 1990.^{21,22}

Because of the increased use of restraints, a decrease in the annual number of motor vehicle fatalities among young children would have been expected. However, the expected decline did not occur. Based on vital statistics mortality data, the number of deaths for child passengers under age five in motor vehicle crashes increased more than 30% between 1984 and 1989. This increase was reason enough to ask whether laws designed to prevent mortality by requiring children to ride in car seats led to increases in traffic fatalities for young children.

Data from the Fatal Accident Reporting System (FARS) can be used to help answer this important policy question. The FARS data classify child deaths from motor vehicle crashes according to whether or not the child was in a safety seat.

Figure 3 shows death rates for children under age five calculated by combining FARS data with data from the Occupant Protection Survey (OPS) and census population figures. The OPS gives an estimate of the proportion of children who were restrained while riding in motor vehicles in each year.

Combining this estimate with population estimates from the census provides an estimate of the number of children who were and were not restrained each year. These data and the FARS data on deaths of children who were and were not in safety seats yield estimates of the death

rates per 100,000 children according to restraint status. And, illustrated in Figure 3, death rates among restrained children remained very flat, changing only slightly between 1984 and 1990, suggesting that the laws requiring safety seats were justified.

Children in safety seats were as safe in 1990 as they had been in 1984, and death rates among children from motor vehicle crashes probably would have been even higher in the mid- to late-1980s if the use of restraints had not been legally mandated.

The failure of the vital statistics data to detect a decrease in child mortality following the legal requirement mandating safety seat use appears to be largely due to the dramatic increase in the death rate for nonrestrained children (the upper line in Figure 3) in the mid-1980s. The increase is likely due to a number of factors that increased the risk for all children riding in motor vehicles during this time period but which particularly affected those who were not restrained.

The National Highway Traffic Safety Administration (NHTSA) studied several potential contributors to the overall increase in child deaths in motor vehicle crashes. This study concluded that deaths increased because (1) children spent more time in cars and (2) children were more likely to be in vehicles involved in crashes.^{23,24}

Children spent about 18% more time in vehicles during 1988 than they had in 1984.²⁵ With increased time in cars came an elevated chance for involvement in a crash, which explains much of the rise in the number of deaths.

In addition, the NHTSA found that children were in more car crashes in 1988 than in 1984. During 1982, children under the age of five were involved in approximately 2,350 motor vehicle crashes. During 1989, they were involved in 3,000 crashes, a nearly 30% increase. This increase in crash involvement is not well understood. It could be due to a

change in driving patterns, increased speed limits on rural highways,²⁶ the greater amounts of time children spent in motor vehicles,²⁵ or simply an increase in the number of children. In any event, the fact that more children were involved in car crashes would, other things being equal, result in an increase in the number of child fatalities from motor vehicle crashes. The introduction of car seats during this time prevented the number of deaths from climbing even higher.²⁷

The child safety seat example shows that standard data sources, such as vital statistics mortality, do not always show the true effects of a particular intervention. Further analysis using other data sources is sometimes required. In addition, this example illustrates the difficulties in making direct comparisons between interventions and outcomes (in this instance, motor vehicle fatalities) of interest.

Determining the cause of a change in fatalities is key to preventing fatalities and serious injuries in the future.

Conclusion

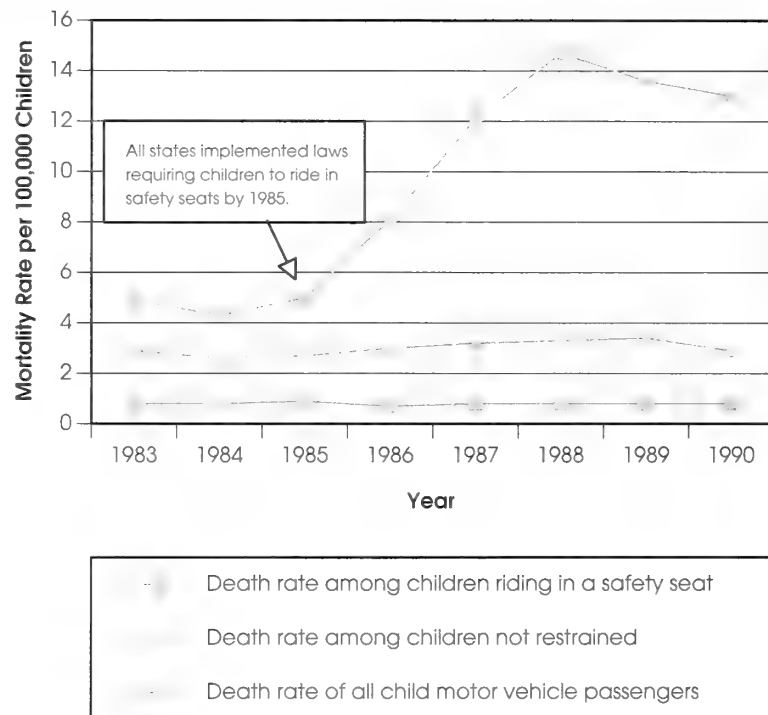
For the past few decades, unintentional injuries have been the leading cause of death and disability for children older than age one in this country. Prevention of those injuries is of critical importance to those interested in the health and well-being of children.

Understanding the origins of unintentional injuries and measuring their impact are key parts of the prevention process. Correctly understood and used, measurements of the causes and results of unintentional injuries will assist in determining what the problems are and how they can best be solved.

Documenting the effectiveness of prevention programs is not always straightforward. Sometimes, detailed examination of the data and the context of the program is required to understand the potentially confounding effects of factors other than the prevention strategy. However, prevention strategies used but

Figure 3

Motor Vehicle Occupant Death Rates for Children Ages 0 through 4 Years, 1983 to 1990



Death rates in this graph were calculated by the authors using data from several sources, including the Fatal Accident Reporting System (FARS), the vital statistics system, a survey of occupant protection in motor vehicles in 19 cities, and population data from the census. The overall death rates are calculated from counts of the number of deaths and the total number of children in the population each year. For the restraint-specific death rates, the number of deaths in each restraint category is used along with the proportion of children restrained in safety seats or seat belts in the overall population of children.

- By 1985, all states had implemented laws requiring children to ride in safety seats when in motor vehicles. The expected result, a decrease in the overall death rate (middle line, above), did not occur.
- When the data are adjusted by the proportion of children who are riding in car seats, the picture is different. The death rate for children in safety seats is stable and much lower than the death rate for nonrestrained children. The laws requiring use of safety seats appear beneficial.
- Use of vital statistics death rates alone (middle line) without the addition of data from other sources presents a misleading picture of the child passenger death rates in the context of child safety seats.

Sources: Unpublished data from the Fatal Accident Reporting System, National Highway Traffic Safety Administration, Washington, DC; Centers for Disease Control and Prevention; Child passenger restraint use and motor-vehicle-related fatalities among children—United States, 1982–1990. *Morbidity and Mortality Weekly Report* (August 30, 1991) 40,34:600–602; U.S. Bureau of the Census. *U.S. population estimates by age, sex, race, and Hispanic origin: 1980 to 1991*. Current Population Reports, Series P-25, No. 1095. Washington, DC: U.S. Government Printing Office, 1993, Table 1; National Center for Health Statistics. *Vital statistics of the United States*. Vol. II. Washington, DC: U.S. Government Printing Office, (1983 through 1989.) Table 5-2; Unpublished data from the Mortality Branch of the National Center for Health Statistics, Washington, DC.

not evaluated cannot show their effectiveness and are more difficult for others to adopt credibly. Measurement is important only insofar as it informs the policymaking process. The purpose of data collection is understanding, so that events leading to unintentional injuries

can be changed, and the injuries themselves can be prevented.

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1. Guyer, B., and Ellers, B. Childhood injuries in the United States: Mortality, morbidity, and cost. *American Journal of Diseases of Children* (June 1990) 144:649–52.
2. National Center for Health Statistics. *Advance report of final mortality statistics, 1991*. Monthly Vital Statistics Report, Vol. 42, No. 2, Suppl. Hyattsville, MD: Public Health Service, 1993.
3. Rivara, F. Traumatic deaths of children in the United States: Currently available prevention strategies. *Pediatrics* (1985) 75:456–62.
4. Children's Safety Network. *A data book of child and adolescent injury*. Washington, DC: National Center for Education in Maternal and Child Health, 1991, p. 15.
5. Harborview Injury Prevention and Research Center, Seattle, WA. Correspondence with Frederick Rivara, October 25, 1994.
6. In some instances, however, the prevention measure may be the same for unintentional and intentional injuries. For example, removing firearms from the home would prevent both intentional and unintentional gunshot injuries.
7. McClain, P.W., Sacks, J.J., Froehle, R.G., and Weigman, B.G. Estimates of fatal child abuse and neglect, United States, 1979 through 1988. *Pediatrics* (February 1993) 91,2:338–43.
8. National Center for Health Statistics, Registration Methods Branch, Division of Vital Statistics. Telephone conversation with George Gay, October 28, 1994.
9. See note no. 2, National Center for Health Statistics, p. 21, Table 6.
10. U.S. Department of Transportation, National Highway Traffic Safety Administration. *Fatal Accident Reporting System*. Washington, DC: NHTSA, no date. Copies of this brochure are available from the National Highway Traffic Safety Administration, Publications Office, 400 7th St., S.W., Washington, DC 20590.
11. Centers for Disease Control. Injury mortality atlas of the United States, 1979–1987. *Morbidity and Mortality Weekly Report* (December 13, 1991) 40,49:846–48.
12. Gallagher, S.S., Finison, K., Guyer, B., and Goodenough, S. The incidence of injuries among 87,000 Massachusetts children and adolescents: Results of the 1980–81 statewide childhood injury prevention program surveillance system. *American Journal of Public Health* (December 1984) 74,12:1340–47.
13. Rivara, F.P., Calonge, N., and Thompson, R.S. Population-based study of unintentional injury incidence and impact during childhood. *American Journal of Public Health* (August 1989) 79,8:990–94.
14. National Committee for Injury Prevention and Control. *Injury prevention: Meeting the challenge*. New York: Oxford University Press, 1989, p. 38. Supplement to the *American Journal of Preventive Medicine* (1989) 5,3.
15. *Setting the national agenda for injury control in the 1990s: Third national injury control conference*. Washington, DC: U.S. Department of Health and Human Services, April 1992, p. 107. Position papers from the conference. April 22–25, 1991, Denver, CO.
16. *Questions commonly asked about E codes*. Produced for the Injury Control and Emergency Health Services Section of the American Public Health Association. Newton, MA: Education Development Center, Inc., 1993. This insert and the brochure it accompanies, *E codes: The missing link in injury prevention*, are available from EDC, 55 Chapel St., Newton, MA 02158-1060.

17. Educational Development Center, Inc., Newton, MA. Telephone conversation with Susan Gallagher, October 24, 1994.
18. Graham, J.D., ed. *Preventing automobile injury: New findings from evaluation research*. Dover, MA: Auburn House, 1988.
19. Kahane, C.J. *Evaluation of child passenger safety: The effectiveness and benefits of safety seats*. National Highway Traffic Safety Administration Report No. DOT-HS-806-890. Washington, DC: NHTSA, February 1986.
20. U.S. Department of Transportation, National Highway Traffic Safety Administration. *Occupant protection trends in 19 cities*. Washington, DC: NHTSA, 1991.
21. Restraint use is defined as use of any restraint device, including seat belts and child safety seats. Data were collected in the now-discontinued Occupant Protection Survey, which used observational techniques to count the number of children under age five who were restrained. (National Highway Traffic Safety Administration. Telephone conversation with Cheryl Neverman, October 27, 1994.)
22. Centers for Disease Control and Prevention. Child passenger restraint use and motor-vehicle-related fatalities among children—United States, 1982–1990. *Morbidity and Mortality Weekly Report* (August 30, 1991) 40,34:600–602.
23. Chorba, T.L., and Klein, T.M. Increases in crash involvement and fatalities among motor vehicle occupants younger than 5 years old. *Pediatrics* (May 1993) 91,5:897–901.
24. Klein, T.M., Van Dyke, J., Surti, J., and Walz, M. *An investigation of the increase in child passenger fatalities since 1984*. National Highway Traffic Safety Administration Report No. DOT-HS-807-701. Washington, DC: NHTSA, September 1990.
25. National Highway Traffic Safety Administration. Telephone conversation with Susan Partyka, October 25, 1994.
26. From 1974 to 1982, all states had upper speed limits of 55 miles per hour. In 1982, legislation was passed permitting 20 states to participate in a demonstration program allowing speed limits of 65 miles per hour on rural highways. In 1987, new legislation was passed allowing all states to have the 65 miles per hour speed limit on rural highways. (Federal Highway Administration. Telephone conversation with Julie Cirillo, October 27, 1994.)
27. Not surprisingly, parents and caretakers who restrained children while riding in motor vehicles appear to be safer drivers than those who did not restrain their children. Comparison of data from the Occupant Protection Survey (OPS) and Fatal Accident Reporting System (FARS) shows that children involved in crashes were less likely to be restrained than those not involved in crashes. In 1990, for example, about 83% of infants in the general population were restrained in some way while riding in motor vehicles, as measured by the OPS. In the same year, the FARS indicates that only 57% of infants in crashes that were fatal for someone involved were restrained. (See note no. 21.) This difference, however, could not account for the increase in overall child mortality from motor vehicle crashes. It also appears that an increase in driving under the influence of alcohol could not have contributed to the rise in child mortality from motor vehicle crashes because, during this time period, there was a gradual decline in the proportion of traffic fatalities that were related to alcohol use. (Unpublished data from the Fatal Accident Reporting System, National Highway Traffic Safety Administration, Washington, DC.)

State Initiatives to Provide Medical Coverage for Uninsured Children

Christopher DeGraw
M. Jane Park
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The Summer/Fall 1993 issue of *The Future of Children* featured an article by Hill, Bartlett, and Brostrom¹ which addressed state initiatives to cover uninsured children. Included were some 15 state-sponsored programs that use either state funding or a combination of state funds plus Medicaid program funds to extend insurance coverage to additional groups of children not eligible for Medicaid. In addition, a new option available to states to expand Medicaid coverage to additional pregnant women and children was discussed.

In the period following that report, comprehensive national health care reform captured center stage in the policy arena. The administration's health security bill and other proposed legislation attempted to provide uniform eligibility requirements, a uniform set of benefits, and financing for health care for adults as well as children. With the demise of comprehensive health care reform at the end of the 103rd Congress, and with bleak prospects for comprehensive legislation in the upcoming session, the focus turns once again to the states.

In this article, the authors examine state level developments affecting health care coverage for children, updating the status of programs reviewed by Hill and colleagues, and describing new initiatives and emerging trends. First, programs ex-

panding insurance coverage for pregnant women and children through Medicaid provisions are reviewed, followed by those involving broader waivers of traditional Medicaid program requirements. Then, examples of state efforts at comprehensive reform are presented, as well as initiatives specifically targeting children and pregnant women.

Medicaid Expansions to Extend Access

Incremental expansions of the Medicaid program continue to be the primary vehicle used by states to extend coverage to additional groups of children and pregnant women. Such expansions often provide the core for more extensive reforms to cover non-Medicaid-eligible populations.

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The Omnibus Budget Reconciliation Act of 1989 mandated states to cover pregnant women and children under age 6 to 133% of the federal poverty level (FPL), with an option to extend up to 185% for pregnant women and infants to age one. In addition, states are required to phase in coverage of children born after September 30, 1983, who have attained age 6 and have family income below 100% FPL. As of October 1, 1994, children at age 11 and younger are covered. By Fiscal Year 2002, all children under 18 with incomes below the FPL will have mandatory Medicaid coverage.

As noted by Hill and colleagues, Section 1902(r)(2), added to the Social Security Act in 1988, effectively gives states the option to liberalize financial eligibility levels for pregnant women and children under the Medicaid program.

There is no upper limit under this option, which involves deducting greater amounts of income and resources when determining program eligibility for these groups than is allowed in determining eligibility for Aid to Families with Dependent Children (AFDC), the method normally used to determine financial eligibility for families with children under Medicaid.

States are using the statutory program options allowing expansion of Medicaid eligibility to pregnant women and infants up to 185% FPL as well as the provisions in Section 1902(r)(2) to further expand coverage for these groups and for older children. By July 1994, 34 states had expanded beyond the 133% level for pregnant women and infants.² For examples of some of the states recently expanding Medicaid coverage for children, see Box 1.

Broader Waivers of Medicaid Rules

In a relatively recent development with significant implications for children, an increasing number of states are seeking broader waivers of Medicaid rules which, in effect, allow them to expand federally funded coverage to adults not normally covered by Medicaid, often in lieu of increasing coverage for additional groups of children.³ While Section 1902(r)(2) offers the states broad options to expand eligibility for the traditional Medicaid program to additional pregnant women and children, other adults—except for the aged, blind, and disabled—cannot be added. As a result, states are requesting waivers of statu-

tory Medicaid requirements to accomplish two basic goals: first, to extend federally assisted Medicaid coverage to both adults and some additional children, and second, to require enrollment of most or all “traditional” and “demonstration” beneficiaries in statewide, full-risk managed care programs that do not necessarily meet existing federal requirements.⁴

A growing number of states are seeking research and demonstration waivers under Section 1115 of the Social Security Act, which permits states to conduct broadly conceived projects that significantly alter Medicaid’s structure, including changing eligibility requirements. Most of the approved Section 1115 demonstrations create statewide managed care systems for some or all traditional Medicaid beneficiaries, including AFDC recipients and low-income pregnant women and children, and in addition, most extend benefits to certain low-income adults who are currently not Medicaid-eligible. In the process, benefits are often modified for both traditional and demonstration eligibles, and states are substituting coverage of adults for coverage of additional children who could have been added without a waiver using Section 1902(r)(2) options.

As of February 1995, eight states have been granted Section 1115 waivers: Florida, Hawaii, Kentucky, Ohio, Oregon, Rhode Island, South Carolina, and Tennessee. Another eight states have requested such waivers from the federal government (Delaware, Illinois, Louisiana, Massachusetts, Minnesota, Missouri, New Hampshire, and Oklahoma), and several others are drafting waiver requests. For examples of state reforms using Section 1115 waivers, see Boxes 2 and 3.

Comprehensive Reforms

A handful of states have been in the forefront of health care reform as they attempt to extend coverage to most, if not all, of the uninsured. Medicaid expansions and state-sponsored children’s insurance programs have often been fundamental to their reform efforts. Among the leaders are Minnesota and Washington. See Table 1.

Special Programs to Cover Children

A number of states have created special programs focusing on populations ineligible for Medicaid and most at risk of being

Box 1

Examples of Recent State Medicaid Expansions

As part of a phase-in of incremental health reforms, **Utah** legislation that took effect July 1, 1994, made all children 12 to 17 years of age in households below the federal poverty level (FPL) eligible for Medicaid.^a The expansion, funded by savings expected from increasing enrollment in capitated health plans, is estimated to extend Medicaid to 32,000 additional children.^b

For the second year in a row, **New Hampshire** extended both age and income eligibility for children under its Medicaid program using Section 1902(r)(2) authority. Medicaid coverage was expanded in 1993 to children 0 to 11 years below 170% of poverty and again in 1994 to include children up to 19 years of age below 185% FPL.^c Coverage of pregnant women increased to 185% FPL in 1994, up from 170% in 1993. The latest expansions took effect July 1, 1994.^d

As part of a package of health care reform bills, **New Mexico** funded Medicaid expansion to children whose family income is less than 185% FPL (approximately \$24,000 for a family of three). It is estimated that the expansions will cover an additional 40,000 children in the first year and 60,000 in the second year.^e

West Virginia passed legislation effective July 1, 1994, to expand Medicaid coverage to as many as 75,000 more children between the ages of 2 and 18 at a cost of nearly \$16 million. By July 1, 1996, the new law will phase in coverage of children in families with incomes of 150% FPL or less. Before passage of the new law, children between the ages of 12 and 18 were covered only if their parents' income was 26% FPL or less. Children from ages 6 to 12 were covered to 100% and those from ages 2 to 6, up to the federally mandated level of 133% FPL.^f The new law also mandates the development of a streamlined Medicaid application form—no longer than two pages—for families applying for coverage for children.^g

In 1993, **Connecticut** expanded Medicaid eligibility using 1902(r)(2) options to children 0 to 6 years below 185% FPL and followed up in 1994 by expanding coverage to children 11 and under below 185% FPL.^c

Healthy Kids, a new program in **Michigan** which expands Medicaid income guidelines, is designed to help children already receiving limited health insurance benefits through a public-private partnership get expanded benefits under Medicaid. The program builds on the Caring Program for Children, begun in 1991 as a Blue Cross/Blue Shield-sponsored, Health Care Financing Administration (HCFA)-funded demonstration, with state and private contributions, to provide a limited package of basic and preventive health care services for children up to 18 years of age with family incomes below 185% FPL.^h The new program will provide full health care benefits under Medicaid to children through age 15 in families with incomes at or below 150% FPL. The Caring Program will continue to provide basic benefits to uninsured children under age 19 who do not qualify for Healthy Kids but whose family incomes are at or below 185% FPL.ⁱ

Sources:

- ^a 1994 Legislative Tracking Service, Intergovernmental Health Policy Project. *Universal coverage and private financing reforms—Quarterly report, October 15, 1994*. Washington, DC: The George Washington University, 1994.
- ^b Bureau of National Affairs. Utah Governor Leavitt signs bills to begin phase-in of health reform. *BNA's Health Care Policy Report* (March 18, 1994) 2:577-78.
- ^c American Academy of Pediatrics, Division of State Government Affairs. *Access—State children's health insurance programs*. Elk Grove Village, IL: AAP, October 20, 1994.
- ^d New Hampshire Division of Human Services, Office of Medical Services. Personal communication with John Fransway, administrator, February 1995.
- ^e Bureau of National Affairs. Reform package of 10 bills sent to governor. *BNA's Health Care Policy Report* (March 7, 1994) 2:459.
- ^f Bureau of National Affairs. Medicaid expansion to cover more children approved by legislature. *BNA's Health Care Policy Report* (March 28, 1994) 2:582.
- ^g Intergovernmental Health Policy Project. *Medicaid and indigent care: Quarterly report, July 15, 1994*. Washington, DC: The George Washington University, 1994.
- ^h Intergovernmental Health Policy Project. *Health care reform: 50 state profiles*. Washington, DC: The George Washington University, July 1994.
- ⁱ Bureau of National Affairs. Michigan children's health plan announced by governor. *BNA's Health Care Policy Report* (July 11, 1994) 2:1239.

Box 2

Rhode Island's Rite Care

One new state program being implemented in part through a Section 1115 waiver focuses almost exclusively on pregnant women and children. **Rhode Island's Rite Care** program, which started enrolling clients August 1, 1994, began with enactment of 1993 legislation that included a mix of insurance and services for women and children, blending Medicaid dollars, state funds, and individual premiums.^a Called by Governor Sundlum "the most significant change in health care delivery in the state" since Medicaid was established, Rite Care expands Medicaid eligibility and provides an enhanced set of primary care and preventive benefits through a fully capitated managed care system.^b Recipients of Aid to Families with Dependent Children (AFDC) and pregnant women and children under age six years with family incomes up to 250% of the federal poverty level (FPL) are eligible. Unlike the traditional Medicaid program, Rite Care requires cost sharing for individuals with family incomes between 185% and 250% FPL. Those below 185% FPL pay \$5 for unauthorized use of emergency services. Participating health plans are required to offer a package of services intended to overcome nonfinancial barriers to care, such as outreach, home visits, nutrition counseling, childbirth education, and parenting classes.^c Rite Care is expected to provide primary health care coverage for 75,000 persons, including 9,000 newly eligible children under age six and several hundred pregnant women, as well as 65,000 current Medicaid recipients.^d

Sources:

- ^a Intergovernmental Health Policy Project. *Major health legislation in the states: '93*. Washington, DC: The George Washington University, January 1994.
- ^b Intergovernmental Health Policy Project. *Health care reform: 50 state profiles*. Washington, DC: The George Washington University, July 1994.
- ^c Bureau of National Affairs. HHS approves Rhode Island program for Medicaid, uninsured populations. *BNA's Health Care Policy Report* (November 15, 1993) 1:1554.
- ^d American Health Line. *50-state report on health reform activities*. Falls Church, VA: AHL, 1994.

uninsured, often using state funds and/or encouraging the private sector to expand coverage to these vulnerable populations. Among the uninsured populations that have received the greatest amount of attention in state legislation are children and pregnant women.⁵ These programs often use state funds to subsidize private insurance coverage. While, unlike Medicaid, these programs do not secure federal matching funds, the state-funded approach avoids the "entitlement" aspects of the Medicaid program as well as its restrictions on eligibility or cost sharing and mandates for specific services. While some state-sponsored initiatives may have benefits identical to the Medicaid program, many state-funded programs for children cover a package of benefits which focuses primarily on prevention and primary care, and does not include inpatient care. Increased availability and use of Medicaid waivers to develop programs to expand coverage for children and other groups have begun to blur the distinctions between purely state-funded and Medicaid-

funded programs. While there have been few new initiatives to cover children, several states are maintaining and, in some instances, expanding existing programs that cover pregnant women and children. For examples of these initiatives, see Table 1.

Extended Coverage Through the Schools

Another recent trend in children's health coverage uses schools to help families access insurance for their children. Florida's Healthy Kids Program, which began as a single county demonstration in 1992 to provide school-based health insurance coverage for uninsured children, has since expanded to six additional counties with a total enrollment of 15,583 children as of February 1995. The program offers a package of benefits through a capitated health maintenance organization (HMO) arrangement to any uninsured child under age 18 in school. Except in Volusia County, where the program was originally implemented with federal funds under a Health

Box 3

Other Section 1115 Programs

Other state programs developed under Section 1115 waivers have not focused exclusively on the maternal and child population. With its waiver granted by the federal government, **Hawaii** began implementing its Health QUEST program designed to provide coverage for all individuals, adults as well as children, with incomes up to 300% of the federal poverty level (FPL) by integrating Medicaid, the State Health Insurance Program, and General Assistance into a single purchasing pool. The program began in summer 1994 and will provide a standard package of benefits through managed care plans.^a

Its 1115 waiver granted in late 1993, **Tennessee's** TennCare program began in January 1994 doing away with the acute care portion of the Medicaid program and substituting a statewide health care reform measure to cover all current Medicaid recipients and the working poor not covered under employer-sponsored health plans through a capitated managed care delivery system that emphasizes prevention. Almost 300,000 previously uninsured residents were enrolled as of July.^a Coverage is free for those under the FPL, with premiums and cost sharing on a sliding scale basis for those between 100% and 200% FPL. Persons above 200% FPL can purchase coverage for the full price of the premium. A survey conducted by the University of Tennessee reported that children under TennCare appear to have visited the doctor more frequently than before the program was instituted.^b

Florida was granted an 1115 waiver in September 1994, which would allow the state to use some \$3.2 billion in federal Medicaid funds to help an estimated 1.1 million uninsured working people and their families purchase private health coverage through the state's 11 Community Health Purchasing Alliances. Under the waiver, which puts Medicaid beneficiaries into managed care programs, savings will be used to fund premium discounts on private insurance coverage on a sliding scale for eligible families who earn too much to qualify for Medicaid, those who do not receive coverage from employers, and those who cannot afford to purchase coverage themselves. As of November 1994, the Florida Health Security Program had not yet been authorized by the state legislature.^c

Sources:

- ^a Intergovernmental Health Policy Project. *Health care reform: 50 state profiles*. Washington, DC: The George Washington University, July 1994.
- ^b Bureau of National Affairs. TennCare beneficiaries happy with plan, see physicians more often, survey finds. *BNA's Health Care Policy Report* (September 19, 1994) 2:1622.
- ^c Bureau of National Affairs. HHS approves Florida waiver to use federal funds for insurance program. *BNA's Health Care Policy Report* (September 19, 1994) 2:1621.

Care Financing Administration demonstration grant and where children in families below 100% FPL have been enrolled free, enrollees pay a sliding scale premium, primarily based on school lunch program status. The additional counties have been funded principally by the state, with local government paying a percentage in matching funds.⁶ The Volusia County program has enrolled about 60% of children who were uninsured prior to the program's implementation.⁷

Based on the Florida model, New Hampshire passed its Healthy Kids Act in 1993, which created a corporation to organize school-based health insurance at up to five pilot sites.⁸ In Kansas, a program to provide insurance to uninsured chil-

dren through school districts, also based on the Florida model, was repealed because of the inability to attract sufficient private funding to operate three demonstration projects.⁵ In addition, in 1994 the Virginia legislature directed its Joint Commission on Health Care to study the feasibility of developing a school-based insurance plan.⁹

Under a new North Carolina law effective July 1994, public schools—through local boards of education—may purchase group health insurance to cover students based on a plan that precludes individual risk selection. The new law allows any insurance company or HMO to offer a low-cost policy for school-age children, focusing on preventive and primary care.

Table 1

Comprehensive State Reforms and Children's Initiatives					
State/Program	Status	Eligibility	Benefits	Financing	Notes
California: <i>Access to Infants and Mothers (AIM)</i> ^a	Ongoing.	Women with incomes above 200% FPL during pregnancy and 60 days postpartum; children 0 to 2 years of age in families with incomes above 200% FPL.	Comprehensive package of inpatient and outpatient services	Cigarette and tobacco revenues (95%) and enrollee premiums (5%).	Program has served some 17,000 pregnant women and 14,000 children since 1992.
Colorado: <i>Children's Health Plan</i> ^b	Expanded in 1993.	Children 0 to 13 years up to 185% FPL.	Well child, outpatient care; some outpatient surgery	Arrangement including state, federal Medicaid, and private funds.	Implemented in 18 counties; almost 1,500 children enrolled as of November 1994.
Connecticut: <i>Healthy Steps</i>	Refunded through June 30, 1995. ^c Limited to demonstration in New Haven.	Children 0 to 14 years in families with incomes under 200% FPL. ^d	Preventive, inpatient, dental, and emergency care; immunizations; outpatient mental health; lab tests ^d	State funds.	Recent evaluation showed the program was cost-effective and resulted in increased access to primary and preventive care. ^e
Delaware: <i>Children's Health Improvement Linkage of Delaware (CHILD)</i> ^f	Network of seven pediatric clinics established statewide to provide primary care. ^g	Medicaid-eligible children covered by capitated fee; uninsured, underinsured Medicaid-ineligible children pay sliding scale fees for clinic services.	Well child care, immunizations, eye exams, corrective lenses, inpatient care	Foundation funds clinic start-up, operations. Under a waiver, Medicaid pays capitated fee for each child enrolled.	As of October 1994, 6,300 children enrolled; clinics had 28,140 visits from 5,777 children (3,000 enrolled in Medicaid managed care).
Massachusetts: <i>Children's Health Security Program</i> ^h	Implemented July 1, 1994, replacing Healthy Kids Program.	Free for children 0 to 12 years with family incomes below 200% FPL; subsidized coverage available for children in families with higher incomes.	Primary and preventive care; mental health and some outpatient surgery	State cigarette tax and enrollee premiums.	Almost 18,000 children enrolled by November 1994. ⁱ

Table 1 (continued)

State/Program	Status	Eligibility	Benefits	Financing	Notes
Minnesota: <i>MinnesotaCare</i> ^l	As of July 1, 1993, all children enrolled in Children's Health Plan transferred to MinnesotaCare.	Children under 18 and adults with children at or below 275% FPL; adults without children up to 125% FPL.	Primary and preventive care; inpatient hospitalization, mental health, and chemical dependency services	Provider tax, enrollee premiums of \$4 per child per month in families to 150% FPL; more than 150% FPL, sliding scale.	42,193 children enrolled as of November 1994.
New York: <i>Child Health Plus</i> ^k	Expanded in June 1994.	Free for children 0 to 15 years in families with incomes below 160% FPL; subsidized for families between 160% and 222% FPL.	Comprehensive outpatient care	Enrollment fees and statewide bad debt and charity care pool.	83,360 children enrolled as of September 1994.
Pennsylvania: <i>Children's Health Insurance Program (CHIP)</i> ^l	Enacted in 1992 and amended in 1994; enrollment began in spring 1993.	Free for children 0 to 13 years up to 185% FPL; premium on sliding scale for children 0 to 5 years between 186% and 235% FPL.	Primary and preventive care; some inpatient care	Paid for by state funds and premiums.	Approximately 35,000 children by fall 1994.
Washington State ^m	Comprehensive reform package passed May 1993; managed competition, individual and employer mandates, cost controls and insurance reforms.	All residents to be covered by 1999 through employer plans, regional purchasing co-ops, state-subsidized Basic Health Plan, and other public programs. Medicaid eligibility expanded July 1, 1994, to 200% FPL.	Uniform benefit package, to be offered by all plans, currently being drafted	Combination of state funding, federal Medicaid funds, premiums, combined with cost control and related measures.	New Medicaid expansions could cover as many as 136,000 additional children.

Sources:

- ^a California Managed Risk Medical Insurance Board. Personal communication with Richard Figueroa, deputy director, November 1994.
- ^b Colorado Child Health Plan. Personal communication with Bonnie Sherman, manager, November 1994.
- ^c Connecticut Healthy Steps Program. Personal communication with Bea Powell, project manager, November 1994.
- ^d American Academy of Pediatrics, Division of State Government Affairs. Access—State children's health insurance programs. Elk Grove Village, IL: AAP, October 20, 1994.
- ^e American Health Line. 50-State report on health reform activities. Falls Church, VA: AHL, 1994.
- ^f The George Washington University Intergovernmental Health Policy Project. State Health Notes (October 18, 1993) 14,166.
- ^g Alfred I. DuPont Institute. Personal communication with Terri Voelker, director of public relations, November 1994.
- ^h Massachusetts Department of Medical Security. The Children's Medical Security Plan: Information about the children's medical security plan. Boston: MDMS, 1994.
- ⁱ Massachusetts Department of Medical Security. Personal communication with Paula Smith, program manager, November 1994.
- ^j Minnesota Department of Human Services. Personal communication with Jeanyne Slettom, public information officer for MinnesotaCare, November 1994.
- ^k Bureau of Community Health and Insurance Finance Systems, New York State Health Department. Personal communication with Steven Dybas, program research specialist, November 1994.
- ^l Bureau of Maternal and Child Health, Pennsylvania Department of Health. A Periodic Update of Pennsylvania's Maternal and Child Health Outreach Program (Fall 1994) 1:2.
- ^m University of Washington, Health Policy Analysis Program. Personal communication with Alice Porter, policy analyst, November 1994.

Premiums may be paid by the board, jointly by the board and the students or family, or by the students (or any other persons on behalf of the students). While school districts have often purchased group accident insurance to cover students, the option to purchase group health insurance for students is a new development in the state.⁹

Other states, including Connecticut, Missouri, and Texas, have recently passed legislation related to expansion of school-based clinics as a way to enhance children's access to health care.⁵

Public-Private Partnerships: Blue Cross/Blue Shield Caring Programs

The Blue Cross/Blue Shield-sponsored Caring Programs for Children have continued to fill gaps in health insurance coverage for children from low-income families who do not meet Medicaid eligibility criteria. Since the report by Hill and colleagues, these programs have been developed in 6 additional states, bringing the total number to 23. Utah's Caring Program, in its third year of operation, provides free coverage for outpatient and preventive care for more than 1,600 low-income children in families whose income is too high to qualify for government health programs but too low to afford health insurance.¹⁰ The Caring Program in Pennsylvania, which was the original Caring Program, in 1994 donated \$2.4 million to provide free primary health coverage to 4,347 additional children in the Western Pennsylvania region, eliminating a seven-month waiting list and raising the number of participating children to more than 7,500. Eligible children are between the ages of 6 and 19, in school, from a family earning not more than 185% FPL, and not eligible for Medicaid or Pennsylvania's state-sponsored Child Health Insurance Program (CHIP).¹¹ The state and Blue Cross/Blue Shield added free mental health benefits and 90 days of hospitalization each year to both Caring Program and CHIP enrollees beginning October 1, 1994.¹² In Kansas, the state continued con-

tributions in 1994 to the Kansas Caring Program for Kids, organized and administered by Blue Cross and Blue Shield of Kansas, the Kansas Medical Society and the Kansas Hospital Association, and largely funded by corporate and individual contributions.⁵ As noted previously, Michigan's new state-sponsored Child Health Insurance Program builds on the Caring Program to provide comprehensive Medicaid benefits to enrollees.

Other Approaches

The West Virginia legislature adopted a measure in 1993 that allows nonprofit organizations to offer loans or vouchers for insurance to encourage low- and moderate-income individuals to use earned income tax credits to buy health insurance for their children.⁵ A similar measure failed to pass in Oklahoma last year.

Outlook

Most observers concede that health care reform is likely to continue to proceed incrementally at both the state and federal levels. When The George Washington University's Intergovernmental Health Policy Project recently surveyed a group of its contacts in state legislatures around the country, most expected their states to take an incremental track, adding targeted populations to coverage plans including expanded, or perhaps universal, coverage for children.⁹ Likewise, at the national level, child health advocates are considering reviving efforts to secure passage of "children first" health care reform legislation. In the meantime, increasing numbers of children will be enrolled in Medicaid managed care programs, and states will continue to seek federal waivers to open subsidized coverage to new groups of beneficiaries. Almost half the states have either been granted, applied for, or are drafting requests for federal Medicaid waivers to restructure their public programs that provide health care coverage to low- and moderate-income residents. In the process, these and other states will be making important policy decisions that will affect children's health care coverage.

1. Hill, I.T., Bartlett, L., and Brostrom, M.B. State initiatives to cover uninsured children. *The Future of Children* (Summer/Fall 1993) 3,2:142-63.

2. NGA Center for Policy Research. *MCH update: State coverage of pregnant women and children—July 1994*. Washington, DC: National Governors' Association, August 1994.
3. The George Washington University Center for Health Policy Research. Medicaid waivers may pose tradeoffs for children. *Health Policy & Child Health* (Fall 1994) 1,4:1–3.
4. Rosenbaum, S., and Darnell, J. *Medicaid Section 1115 demonstration waivers: Approved and proposed activities as of November 1994*. Washington, DC: Kaiser Commission on the Future of Medicaid, November 1994.
5. Intergovernmental Health Policy Project. *Health care reform: 50 state profiles*. Washington, DC: The George Washington University, July 1994.
6. Florida Healthy Kids Corporation. Personal communication with Rose Naff, executive director, February 1995.
7. Institute for Child Health Policy, University of Florida. Personal communication with Betsy Shenkman, coordinator of research, November 1994.
8. Intergovernmental Health Policy Project. *Major health legislation in the states: '93*. Washington, DC: The George Washington University, January 1994.
9. 1994 Legislative Tracking Service, Intergovernmental Health Policy Project. *Universal coverage and private financing reforms—Quarterly report, October 15, 1994*. Washington, DC: The George Washington University, 1994.
10. Bureau of National Affairs. Low-income children receive free care under program sponsored by Utah BCBS. *BNA's Health Care Policy Report* (September 19, 1994) 2:1632.
11. Bureau of National Affairs. Children receiving free primary care increased due to BCBS donation. *BNA's Health Care Policy Report* (January 17, 1994) 2:98.
12. American Health Line. *50-state report on health reform activities*. Falls Church, VA: AHL, 1994.

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The following back issues are available free of charge from the Center for the Future of Children:

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This issue examines the process of divorce and its consequences upon the lives of children and their families. Articles focus on the history of divorce, its financial impact on families, child custody, child support, and children's adjustment to divorce.

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Volume 3, Number 3 (Winter 1993) 216 pp.

Edited by Deanna S. Gomby, Ph.D. and Carol S. Larson, J.D.

This issue examines the use of home visiting programs to serve pregnant women and families with young children. Articles focus on the diversity of home visiting programs and their goals, the use of home health visiting in Europe, the research literature evaluating the effectiveness of home visiting approaches, and the economic evaluation of home visiting programs.

Health Care Reform

Volume 3, Number 2 (Summer/Fall 1993) 216 pp.

Edited by Eugene M. Lewit, Ph.D.

This issue focuses on making health care reform work for children. Articles discuss an appropriate benefits package for women and children, innovative ways of paying for health care services, how to guarantee coverage with multiple insurers, managed care for children and pregnant women, and state programs to expand health insurance coverage.

Adoption

Volume 3, Number 1 (Spring 1993) 184 pp.

Edited by Irving Schulman, M.D.

This issue examines adoption as the primary means of providing a stable, nurturing, loving home to some children who, for a variety of reasons, have been deprived of such an environment. From the perspective of what is in the best interests of the child, the authors explore the major barriers to adoption and an overview of adoption today.

U.S. Health Care for Children

Volume 2, Number 2 (Winter 1992) 192 pp.

Edited by Eugene M. Lewit, Ph.D.

This issue assesses the strengths and weaknesses of the U.S. health care system for children and pregnant women. Written by research and medical experts, articles examine the measurement of health status, the effectiveness of health care, health care services, expenditures on health care for children, public and private insurance, and barriers to access to care.

School-Linked Services

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Edited by Carol S. Larson, J.D.

This issue focuses on the current trend toward having schools coordinate and/or provide health and other social services for children and their families. Contributing authors offer a variety of viewpoints about financing, planning, implementing, and evaluating school-linked services. (Related Working Paper #1932 also available.)

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A Selected Bibliography

1. Burtless, G. Public spending on the poor: Historical trends and economic limits. In *Confronting poverty: Prescriptions for change*. Cambridge, MA: Harvard University Press, 1994, pp. 51–84.
2. Chalmers, I. *Oxford database of perinatal trials*. Version 1.2, Spring 1992 disk issue 7. Oxford: Oxford University Press, 1992.
3. Chalmers, I., Enkin, M., and Keirse, M., eds. *Effective care in pregnancy and childbirth*. Vol. 1. Oxford: Oxford University Press, 1989, pp. 715–21.
4. Hughes, D., Johnson, K., Rosenbaum, S., et al. *The health of America's children: The maternal and child health data book*. Washington, DC: Children's Defense Fund, 1988.
5. Institute of Medicine, Committee to Study Outreach for Prenatal Care. *Prenatal care: Reaching mothers, reaching infants*. Washington, DC: National Academy Press, 1988.
6. Institute of Medicine, Committee to Study the Prevention of Low Birth Weight. *Preventing low birthweight*. Washington, DC: National Academy Press, 1985.
7. Institute of Medicine, Subcommittee on Nutritional Status and Weight Gain During Pregnancy. *Nutrition during pregnancy*. Washington, DC: National Academy Press, 1990.
8. Kramer, M.S. Determinants of low birth weight: Methodological assessment and meta-analysis. *Bulletin of the World Health Organization* (1987) 65:663–737.
9. *March of Dimes statbook: Statistics for healthier mothers and babies*. White Plains, NY: March of Dimes Birth Defects Foundation, 1993.
10. Nathanielsz, P.W. A time to be born. In *Life before birth and a time to be born*. Ithaca, NY: Promethean, 1992, pp. 162–81.
11. National Commission to Prevent Infant Mortality. *Death before life: The tragedy of infant mortality*. Washington, DC: NCPIM, 1988.
12. National Committee on Perinatal Health. *Toward improving the outcome of pregnancy: The 90s and beyond*. White Plains, NY: March of Dimes Birth Defects Foundation, 1993.
13. National Institutes of Health. *NIH Consensus Development Conference on Effect of Corticosteroids for Fetal Maturation on Perinatal Outcomes: February 28–March 2, 1994*. Bethesda, MD: U.S. Department of Health and Human Services, 1994.
14. Paneth, N., Wallenstein, S., Kiely, J., and Susser, M. Social class indicators and mortality in low birth weight infants. *American Journal of Epidemiology* (1982) 116,2:364–75.
15. Rogers, R.G. Living and dying in the USA: Sociodemographic determinants of death among blacks and whites. *Demography* (May 1992) 29,2:287–303.
16. Sexton, M., and Hebel, J.R. A clinical trial of change in maternal smoking and its effect on birth weight. *Journal of the American Medical Association* (1984) 251:911–15.
17. Shiono, P.H., and Klebanoff, M.A. Ethnic differences in preterm and very preterm delivery. *American Journal of Public Health* (1986) 76:1317–21.
18. Sinclair, J.C., and Bracken, M.B., eds. *Effective care of the newborn infant*. Oxford: Oxford University Press, 1992.
19. Society of Critical Care Medicine Ethics Committee. Consensus statement on the triage of critically ill patients. *Journal of the American Medical Association* (1994) 271:1200–1203.
20. The Infant Health and Development Program. Enhancing the outcomes of low-birth-weight, premature infants. *Journal of the American Medical Association* (1990) 263:3035–42.
21. Tyson, J. Dubious distinctions between research and clinical practice using experimental therapies: Have our patients been well served? In *Ethics and perinatology: Issues and perspectives*. A. Goldworth, W.A. Silverman, D.K. Stevenson, and E.W.E. Young, eds. Oxford: Oxford University Press. In press.
22. U.S. Congress, Office of Technology Assessment. *Neonatal intensive care for low birthweight infants: Costs and effectiveness*. Health Technology Case Study 38. OTA-HCS-38. Washington, DC: OTA, 1987.
23. U.S. Department of Health and Human Services. *Health status of minorities and low-income groups*. 3rd ed. Washington, DC: U.S. Government Printing Office, 1991.
24. U.S. Department of Health and Human Services, Public Health Service Expert Panel on the Content of Prenatal Care. *Caring for our future: The content of prenatal care*. Washington, DC: DHHS, 1989.

